FIG. 1

REACTIVITY OF ANTI-FACTOR D MAbs WITH FACTOR D IN ELISA

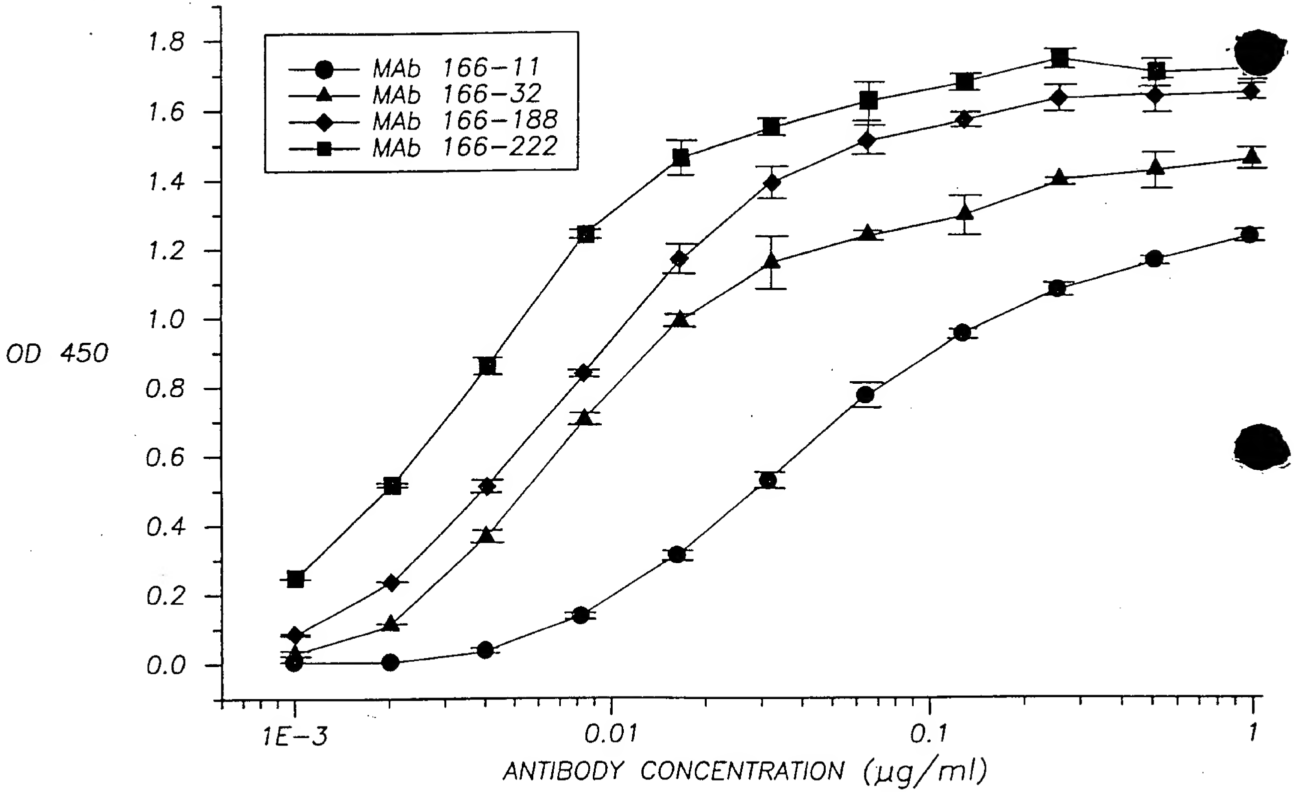

FIG.2

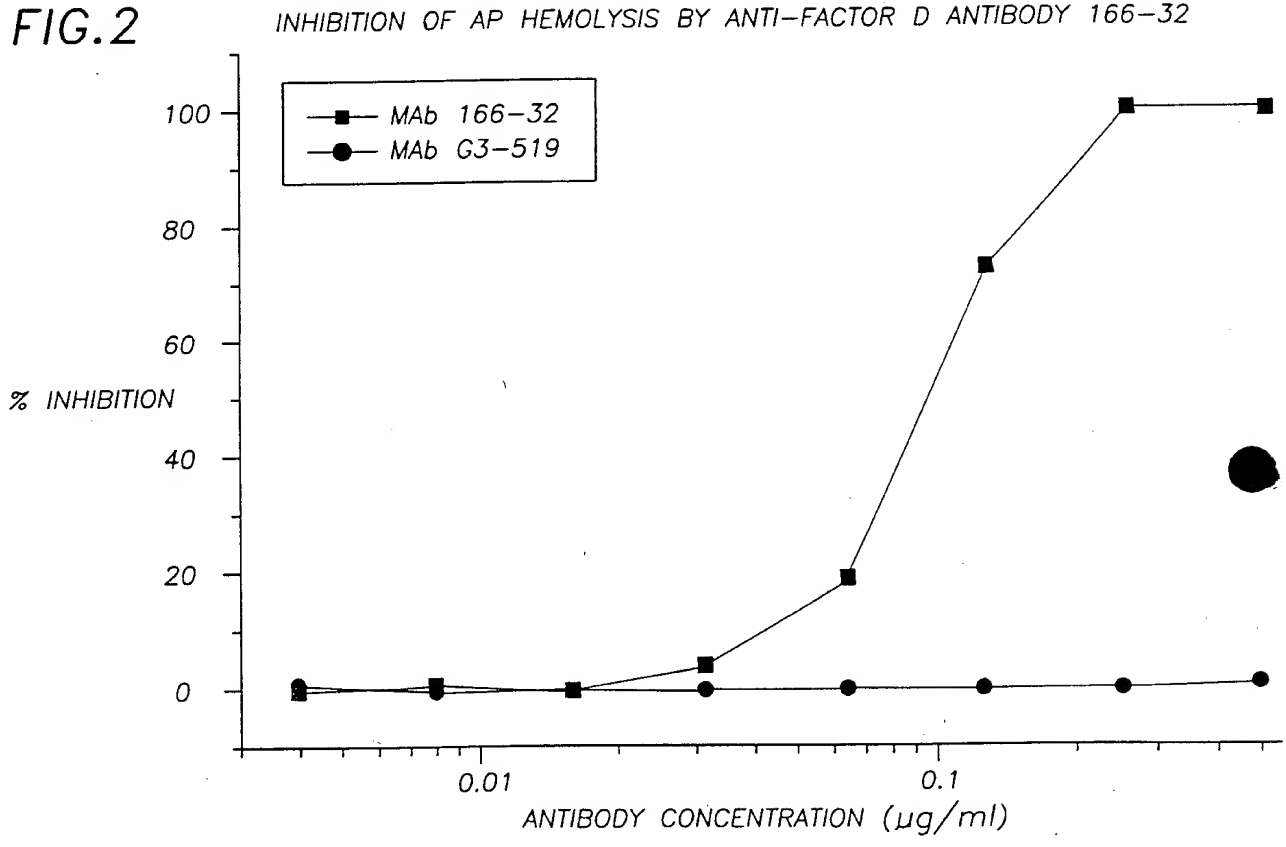

FIG.3

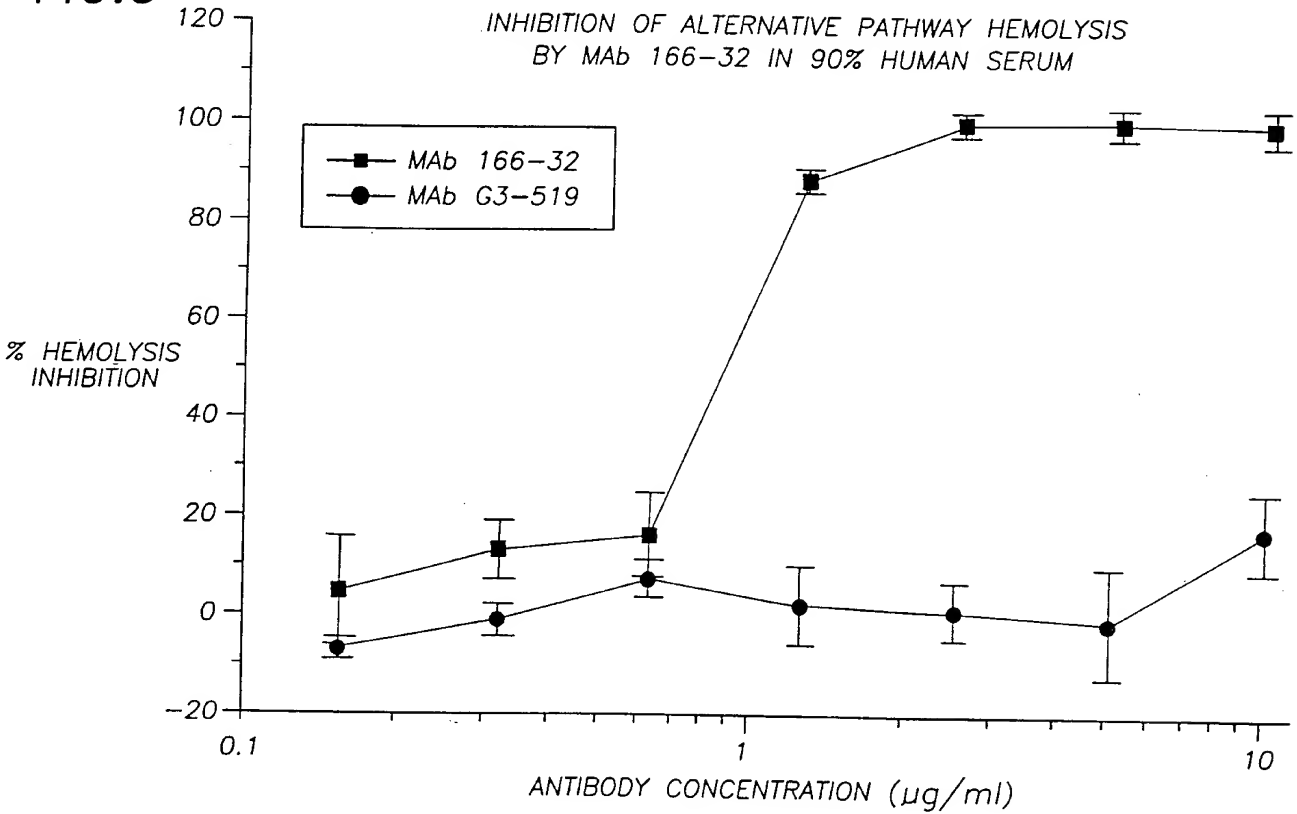

FIG.4

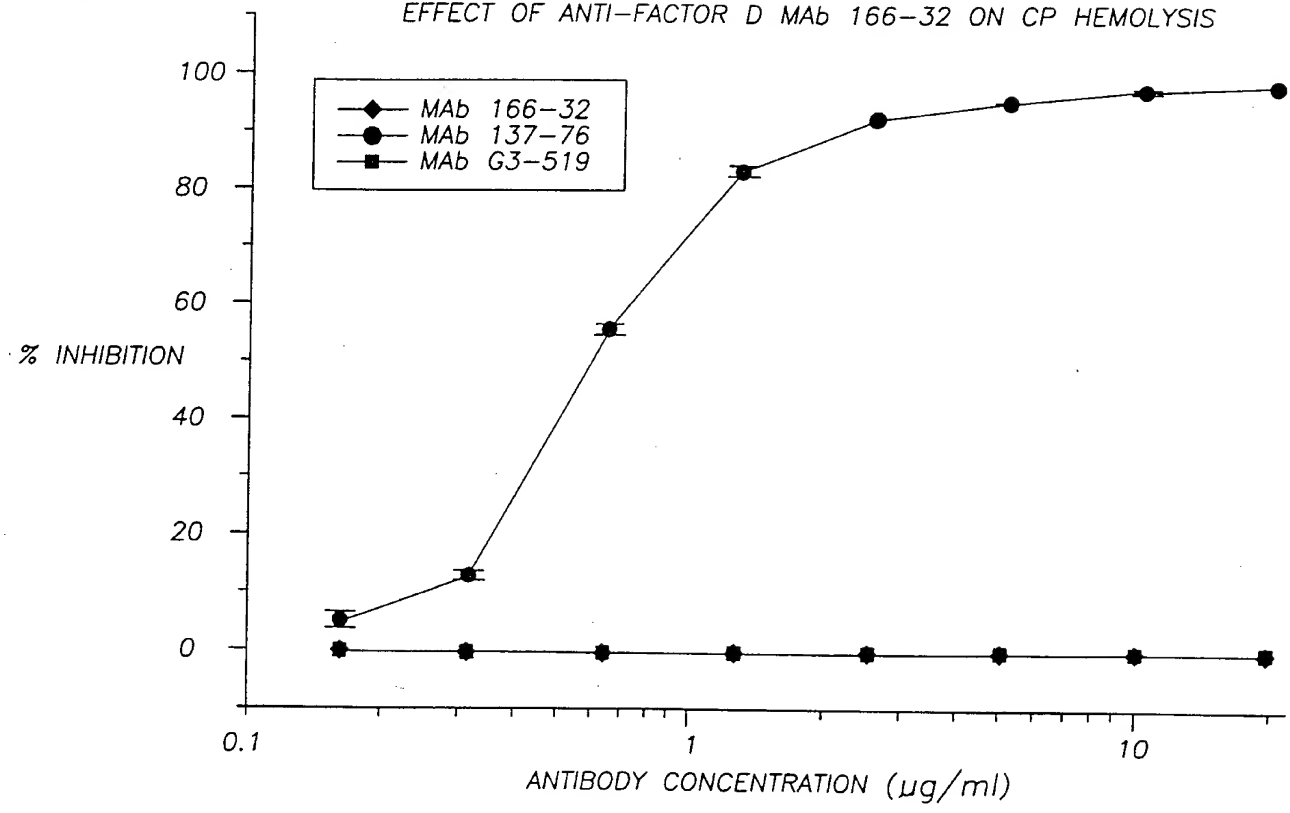
EFFECT OF ANTI-FACTOR D MAb 166-32 ON CP HEMOLYSIS
MAb 166-32
MAb 137-76
MAb G3-519
% INHIBITION
100
80
60
40
20
0
0.1
1
10
ANTIBODY CONCENTRATION (µg/ml)

FIG.5

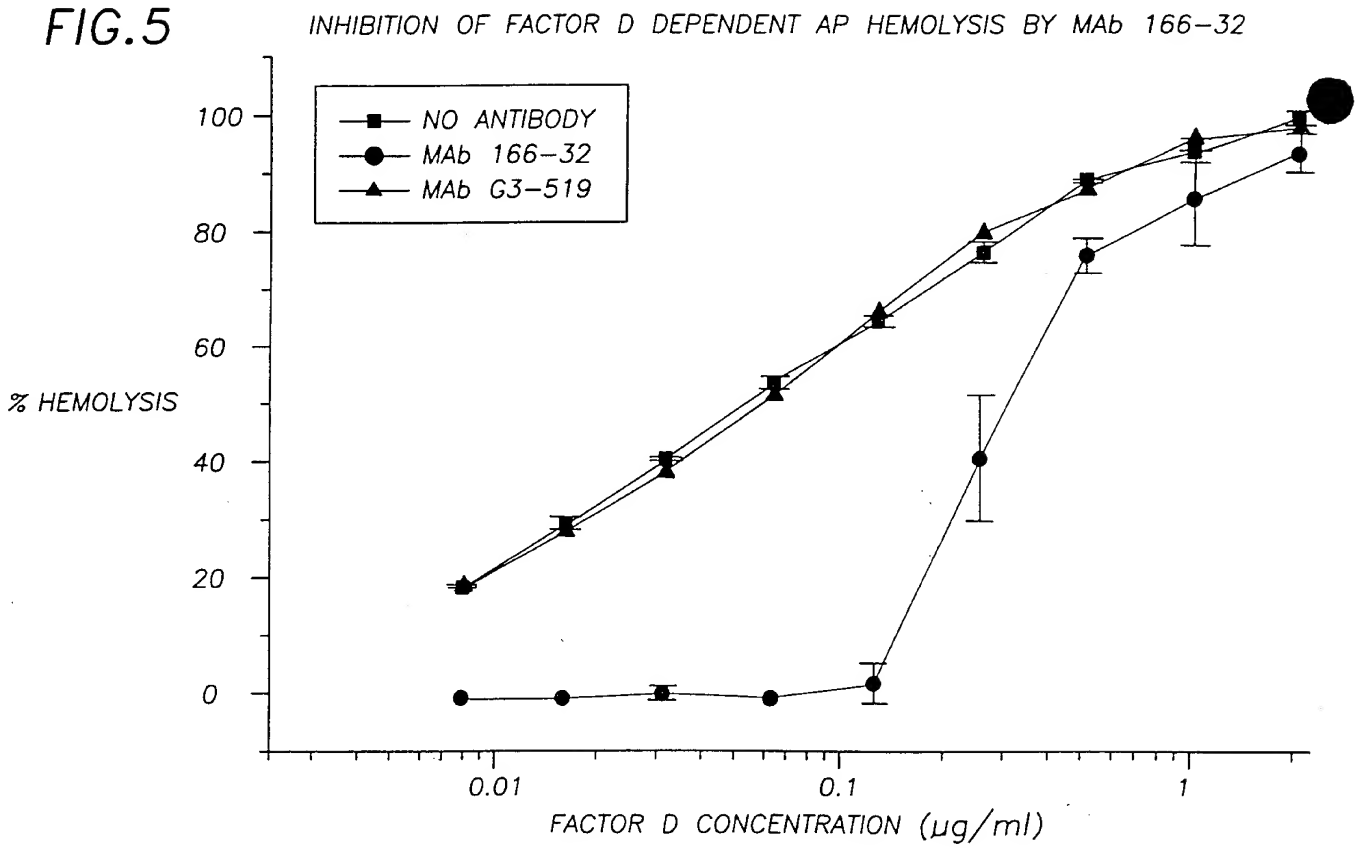

FIG.6

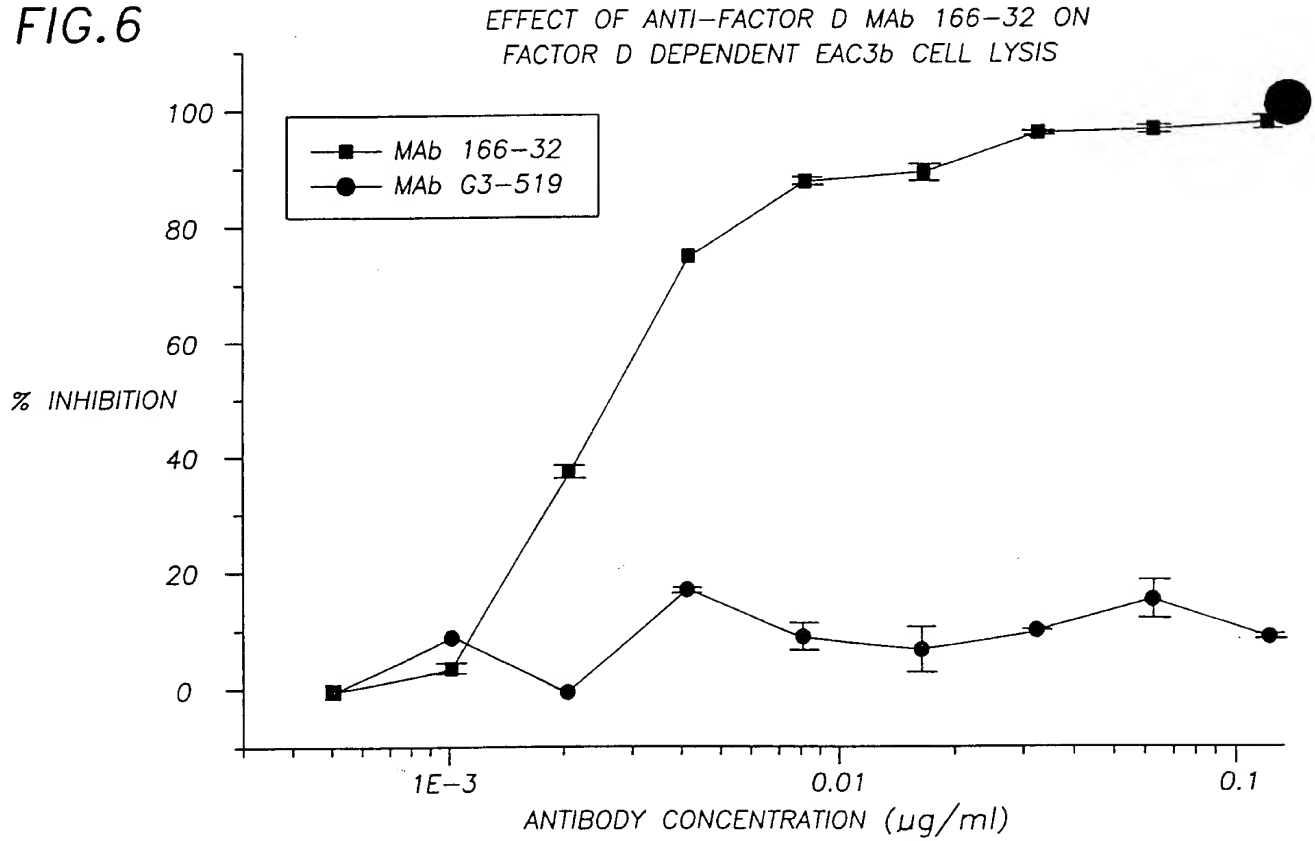
EFFECT OF ANTI-FACTOR D MAb 166-32 ON
FACTOR D DEPENDENT EAC3b CELL LYSIS
MAb 166-32
MAb G3-519
% INHIBITION
100
80
60
40
20
0
1E-3
0.01
0.1
ANTIBODY CONCENTRATION (µg/ml)

FIG.7

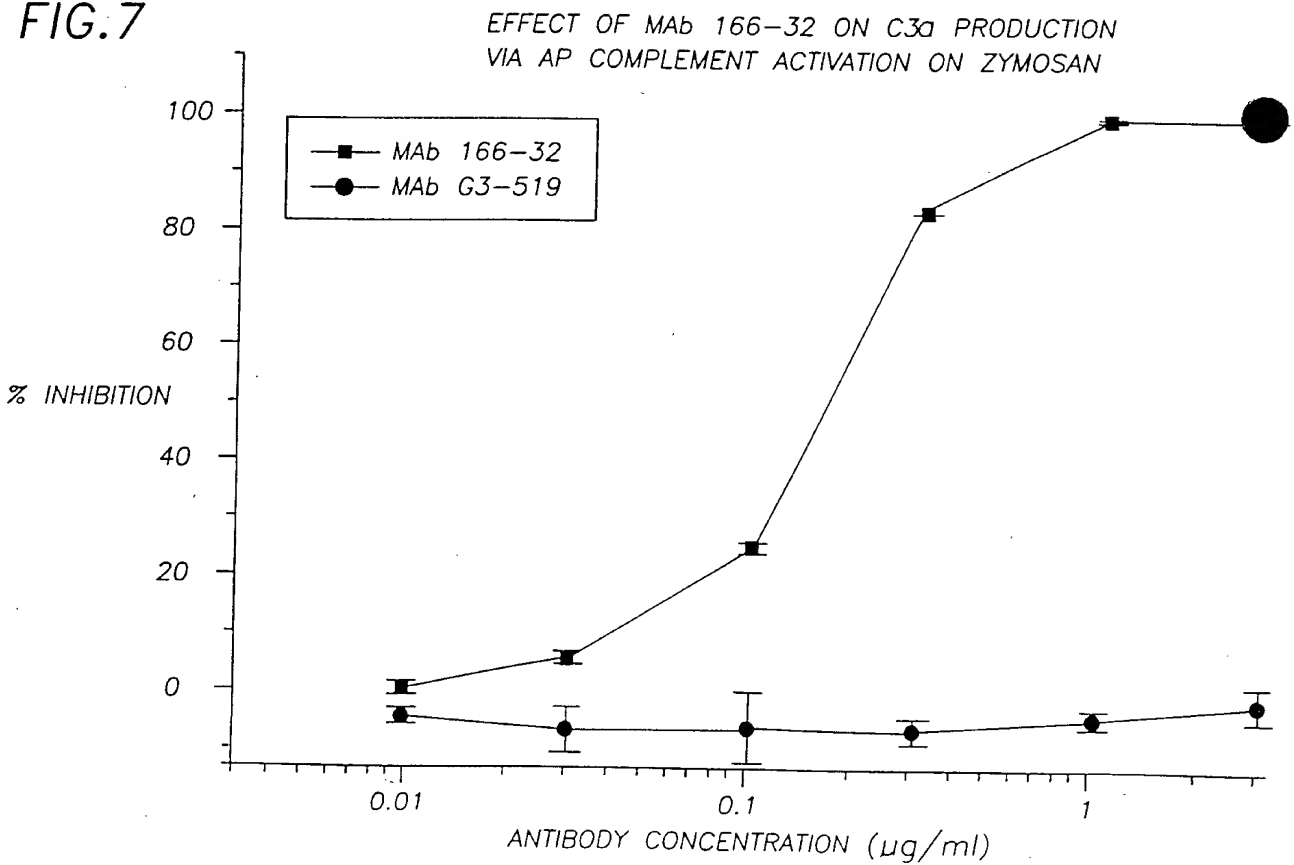
EFFECT OF MAb 166-32 ON C3a PRODUCTION
VIA AP COMPLEMENT ACTIVATION ON ZYMOSAN
MAb 166-32
MAb G3-519
100
80
60
40
20
0
% INHIBITION
0.01
0.1
1
ANTIBODY CONCENTRATION (µg/ml)

FIG.8

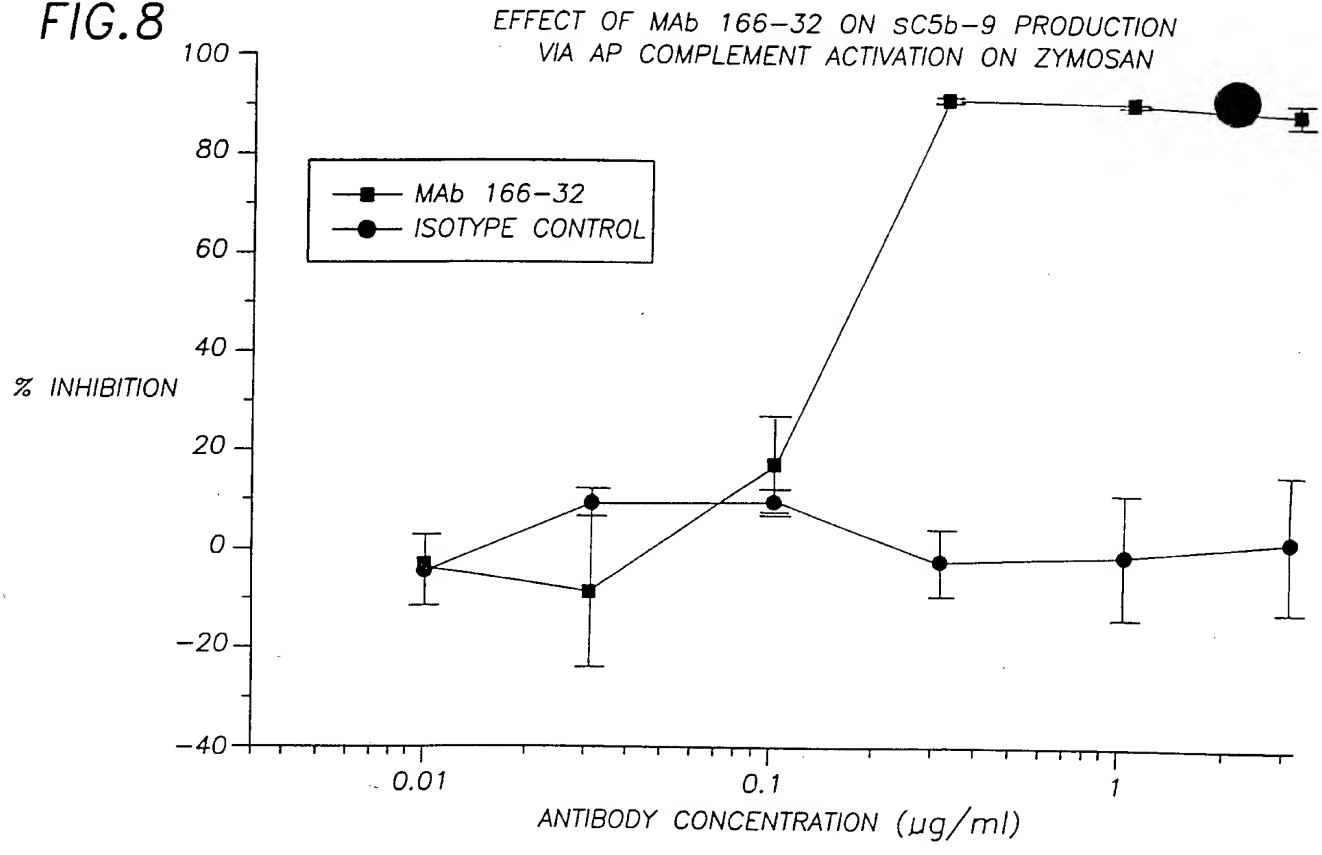
EFFECT OF MAb 166-32 ON sC5b-9 PRODUCTION
VIA AP COMPLEMENT ACTIVATION ON ZYMOSAN
MAb 166-32
ISOTYPE CONTROL
% INHIBITION
100
80
60
40
20
0
-20
-40
0.01
0.1
1
ANTIBODY CONCENTRATION (µg/ml)

FIG.9

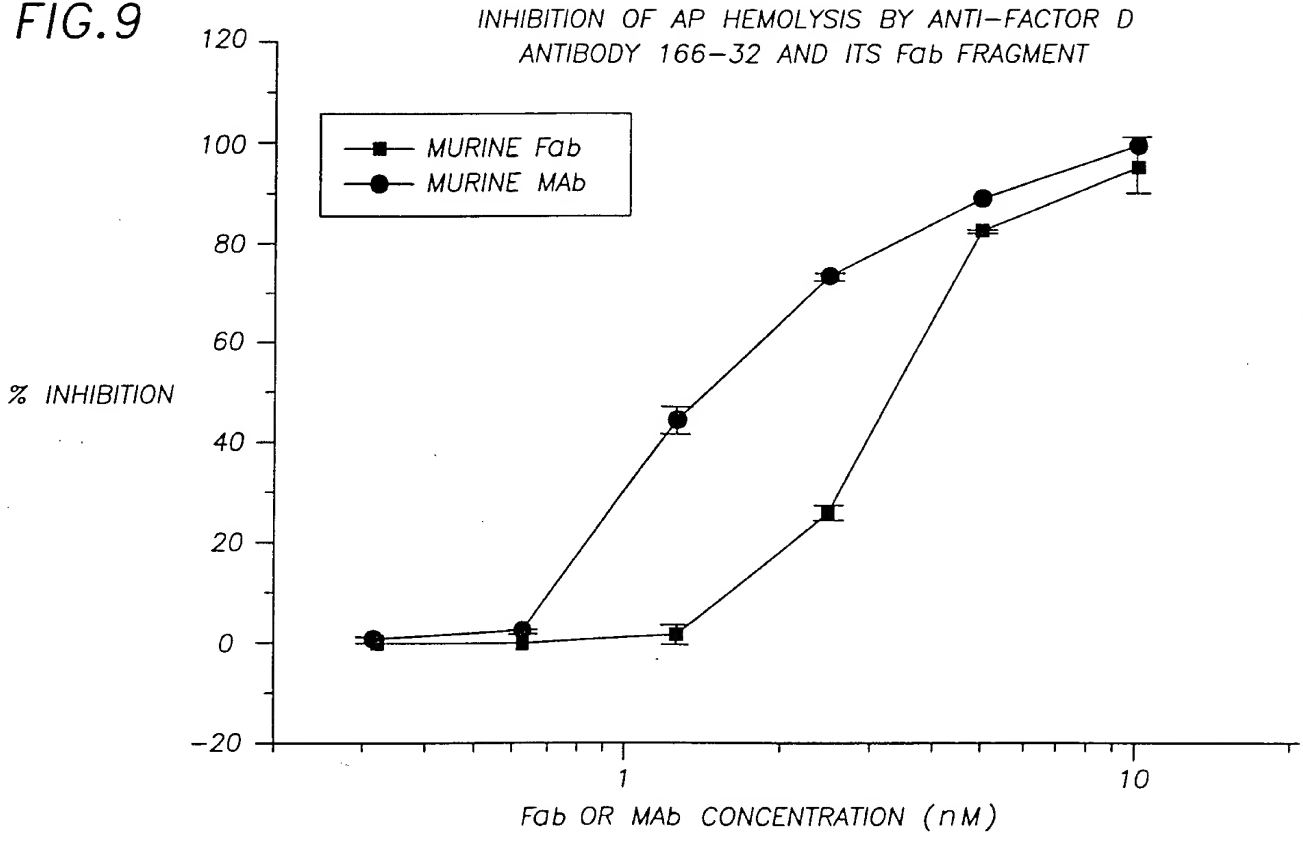
INHIBITION OF AP HEMOLYSIS BY ANTI-FACTOR D ANTIBODY 166-32 AND ITS Fab FRAGMENT
MURINE Fab
MURINE MAb
% INHIBITION
120
100
80
60
40
20
0
-20
1
10
Fab OR MAb CONCENTRATION (nM)

FIG. 10

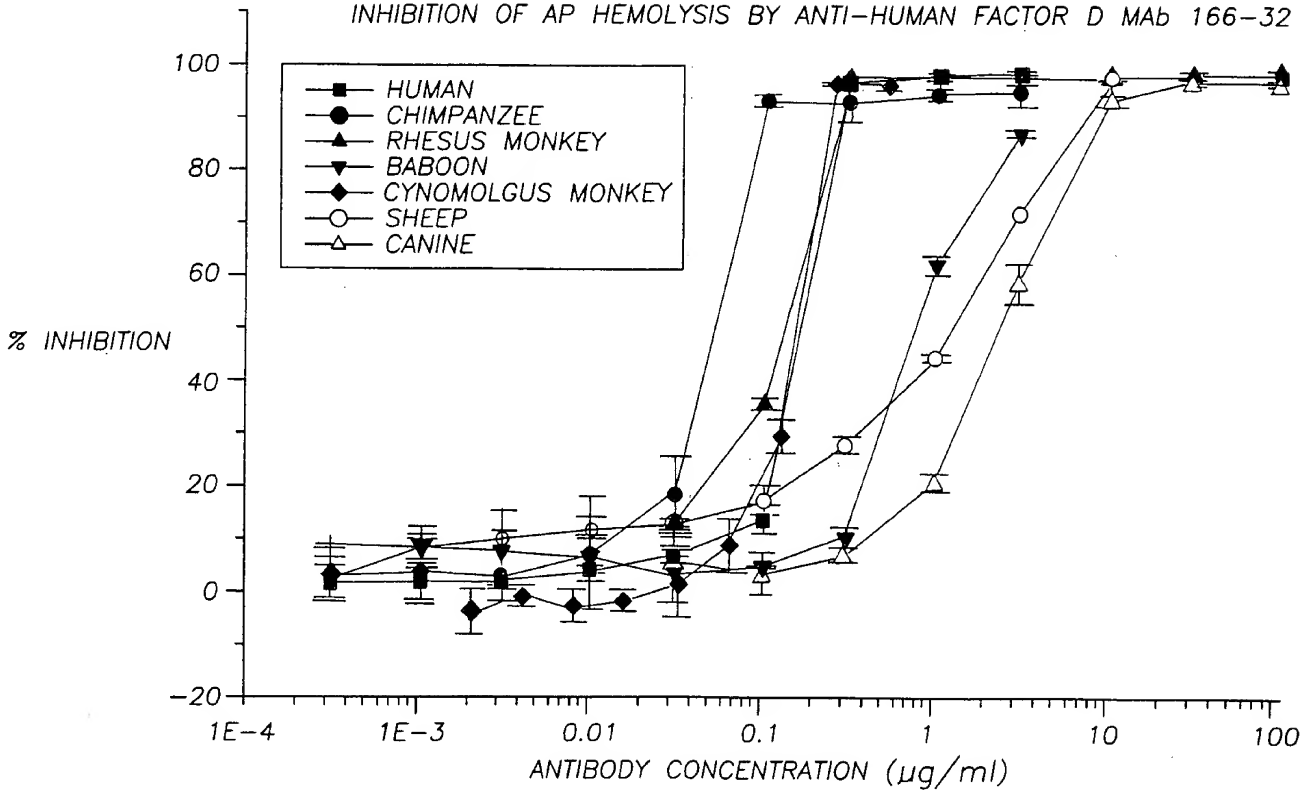
INHIBITION OF AP HEMOLYSIS BY ANTI-HUMAN FACTOR D MAb 166-32
HUMAN
CHIMPANZEE
RHESUS MONKEY
BABOON
CYNOMOLGUS MONKEY
SHEEP
CANINE
% INHIBITION
100
80
60
40
20
0
-20
1E-4
1E-3
0.01
0.1
1
10
100
ANTIBODY CONCENTRATION (µg/ml)

FIG. 11

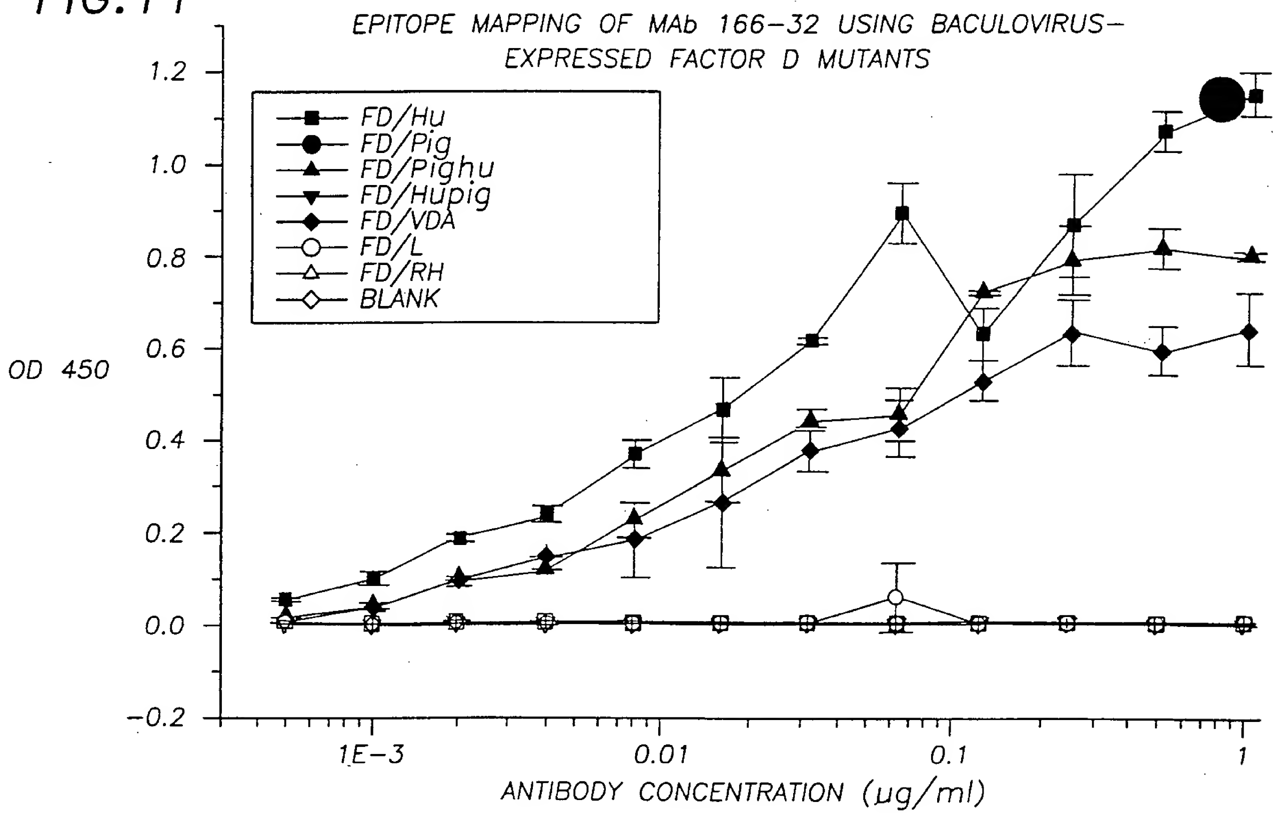
EPITOPE MAPPING OF MAb 166-32 USING BACULOVIRUS-
EXPRESSED FACTOR D MUTANTS
OD 450
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
1E-3
0.01
0.1
1
ANTIBODY CONCENTRATION (μg/ml)
FD/Hu
FD/Pig
FD/Pighu
FD/Hupig
FD/VDA
FD/L
FD/RH
BLANK

FIG. 12

SCHEMATIC REPRESENTATION OF THE EXPRESSION VECTOR PLASMIDS FOR CHIMERIC 166-32 Fab: (A) pSV2dhfrFd AND (B) pSV2neoK

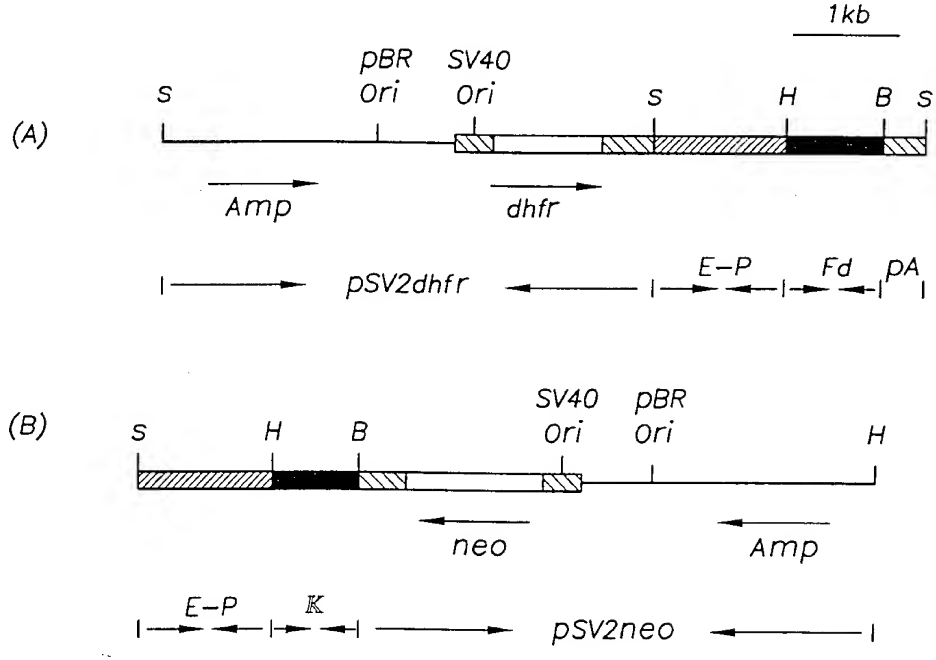

FIG. 13

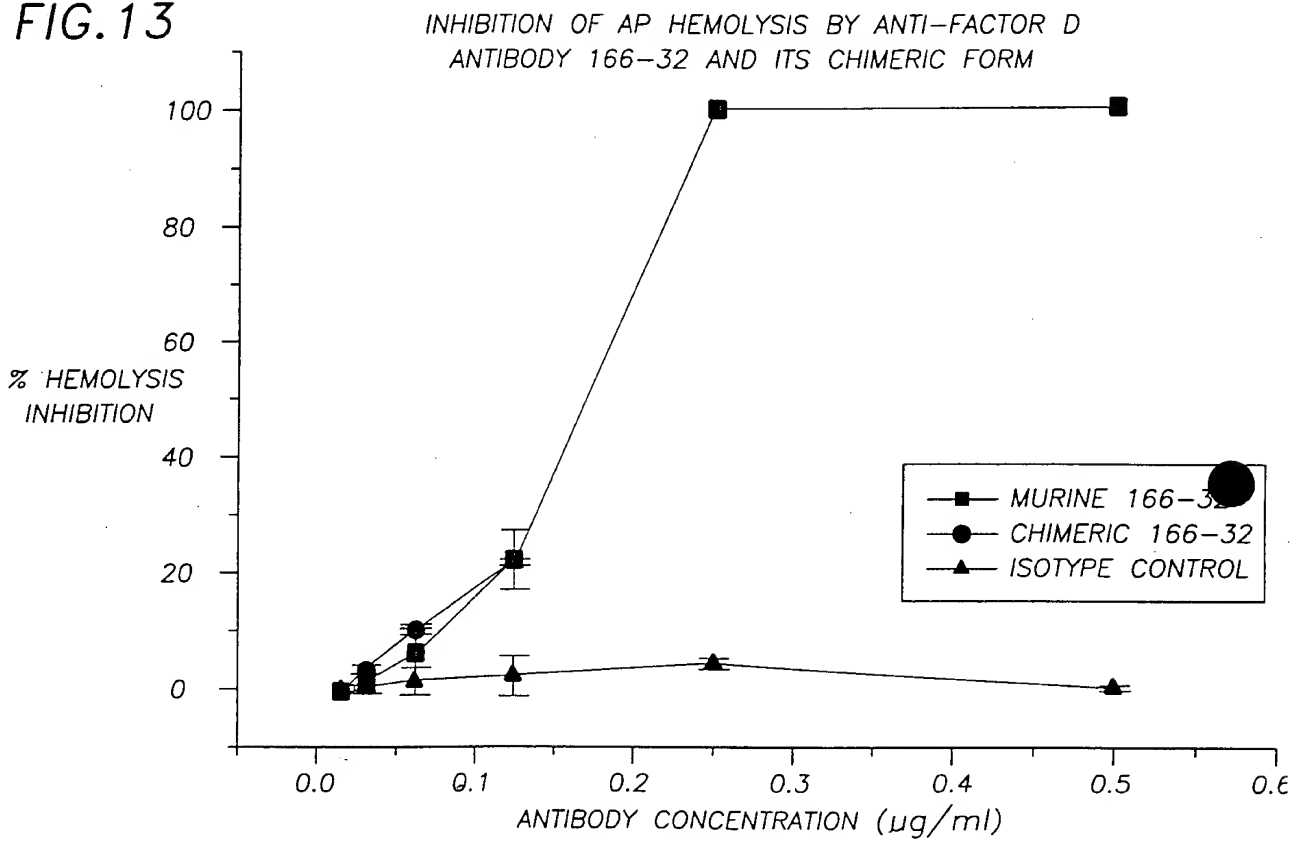
INHIBITION OF AP HEMOLYSIS BY ANTI-FACTOR D ANTIBODY 166-32 AND ITS CHIMERIC FORM
% HEMOLYSIS INHIBITION
100
80
60
40
20
0
0.0
0.1
0.2
0.3
0.4
0.5
ANTIBODY CONCENTRATION (µg/ml)
MURINE 166-32
CHIMERIC 166-32
ISOTYPE CONTROL

FIG. 14

INHIBITION OF AP HEMOLYSIS BY CHIMERIC 166-32 IgG AND ITS Fab

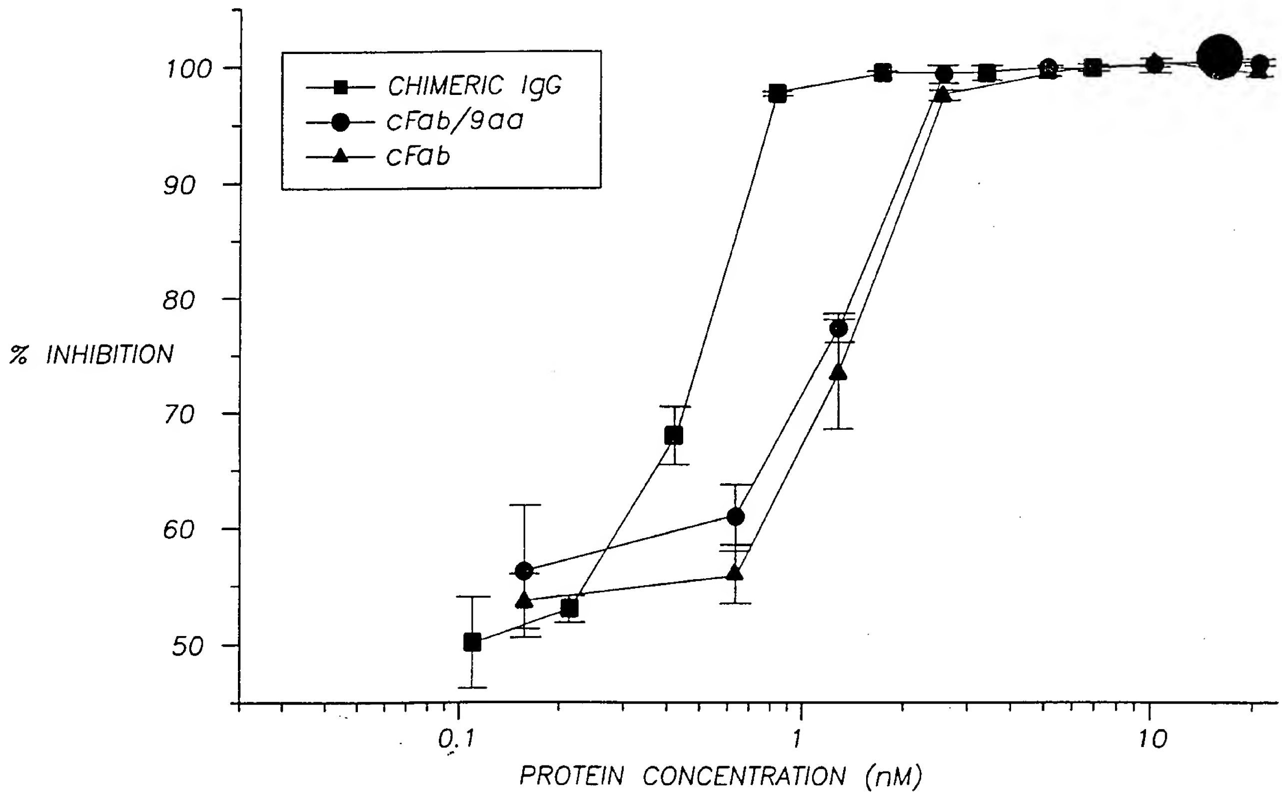

FIG. 15

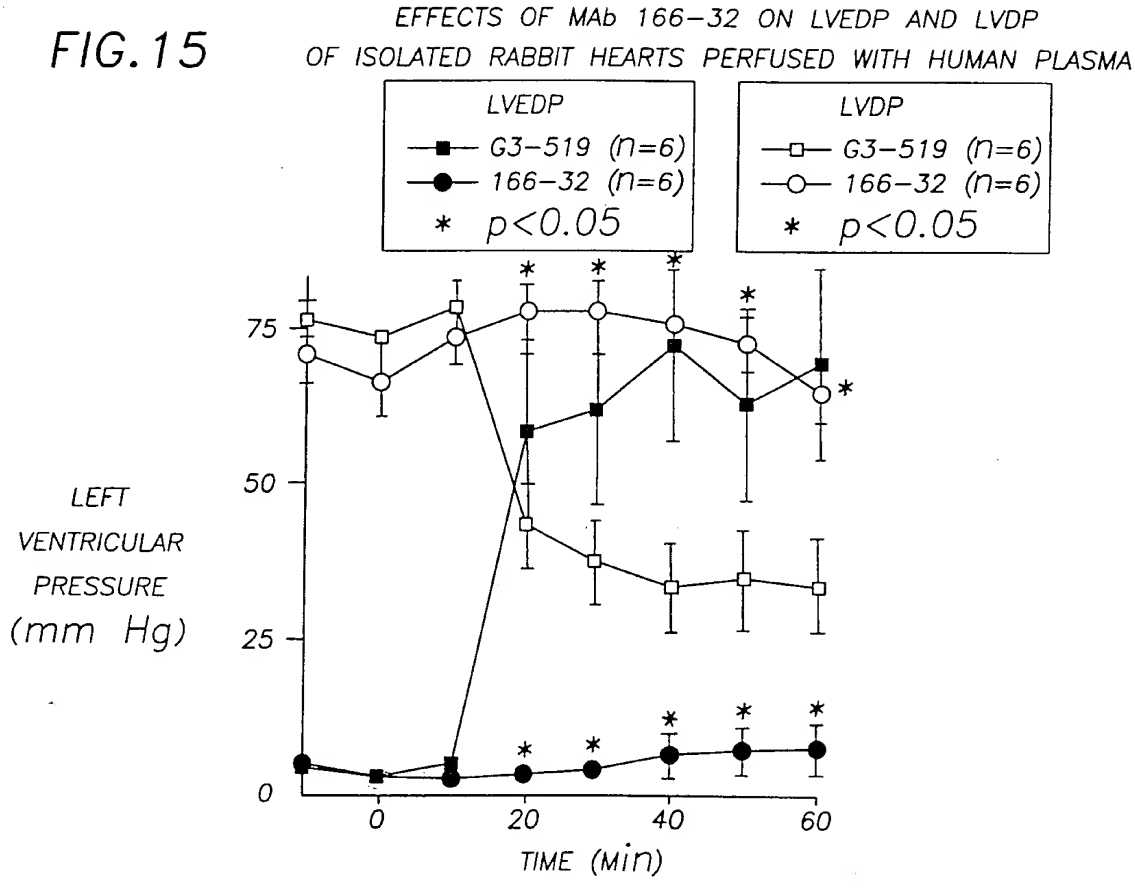
EFFECTS OF MAb 166-32 ON LVEDP AND LVDP
OF ISOLATED RABBIT HEARTS PERFUSED WITH HUMAN PLASMA
LVEDP
G3-519 (n=6)
166-32 (n=6)
* p<0.05
LVDP
G3-519 (n=6)
166-32 (n=6)
* p<0.05
LEFT VENTRICULAR PRESSURE (mm Hg)
75
50
25
0
0
20
40
60
TIME (min)

FIG. 16

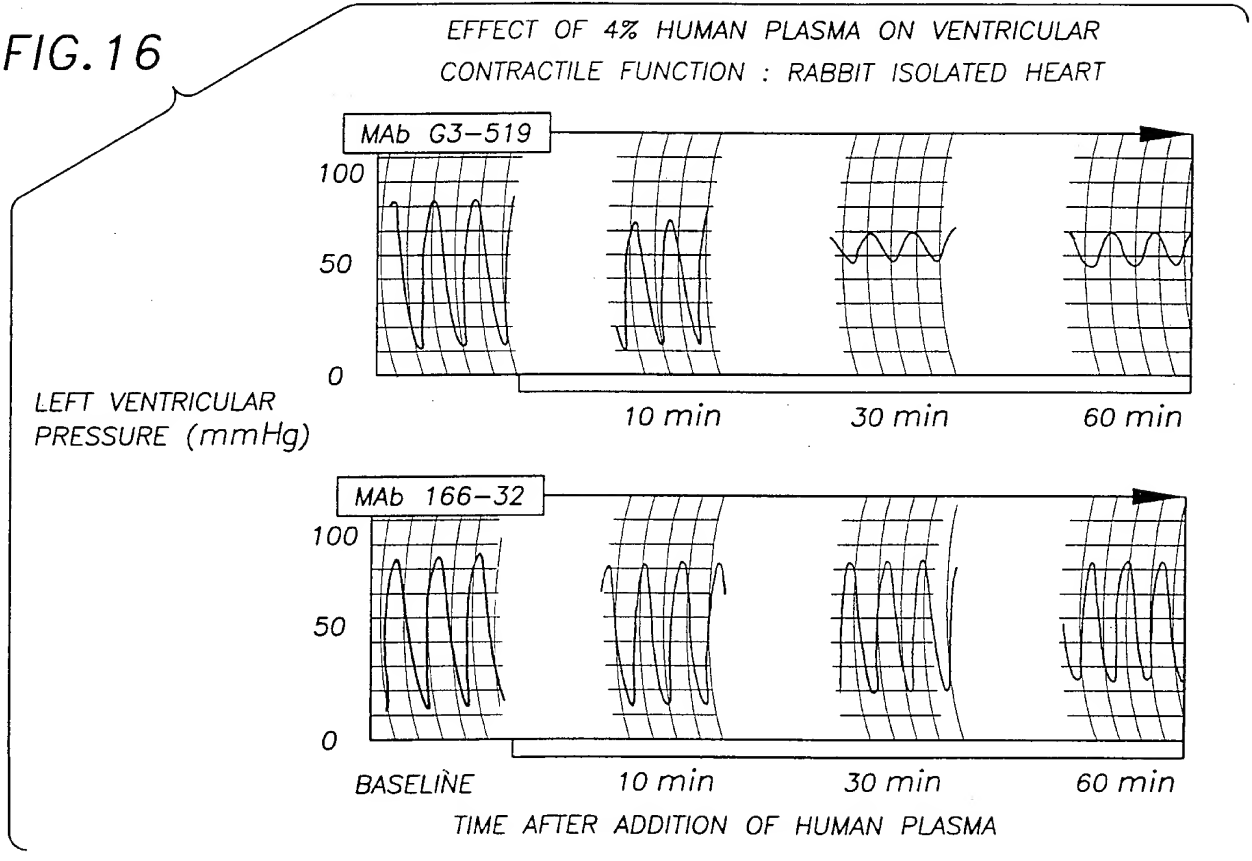

FIG. 17

EFFECTS OF MAb 166-32 ON THE LEVELS OF Bb IN CARDIAC LYMPH OF ISOLATED RABBIT HEARTS PERFUSED WITH HUMAN PLASMA

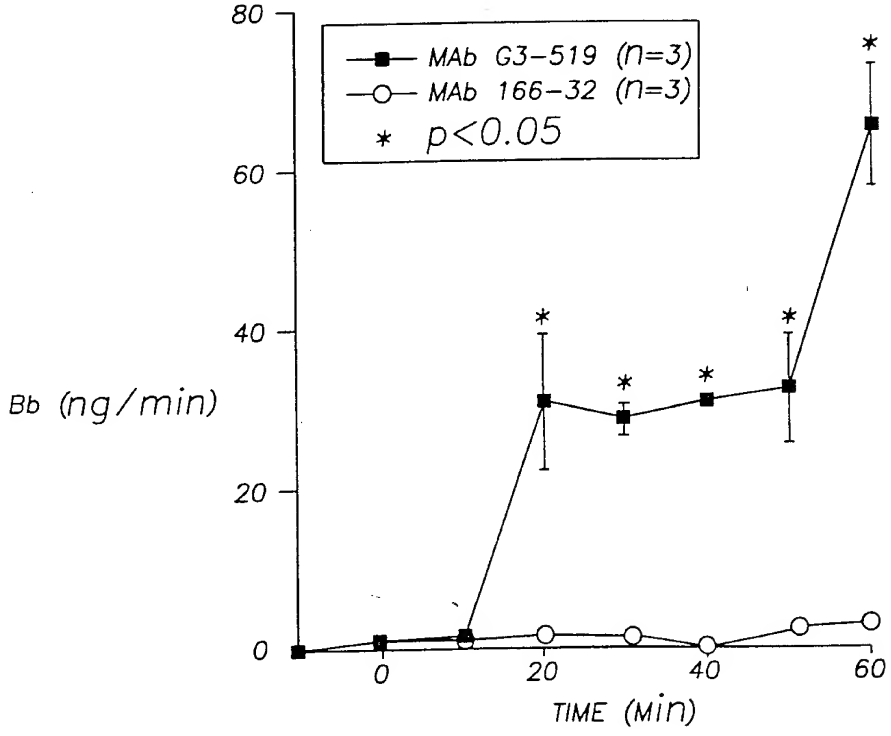

FIG.18

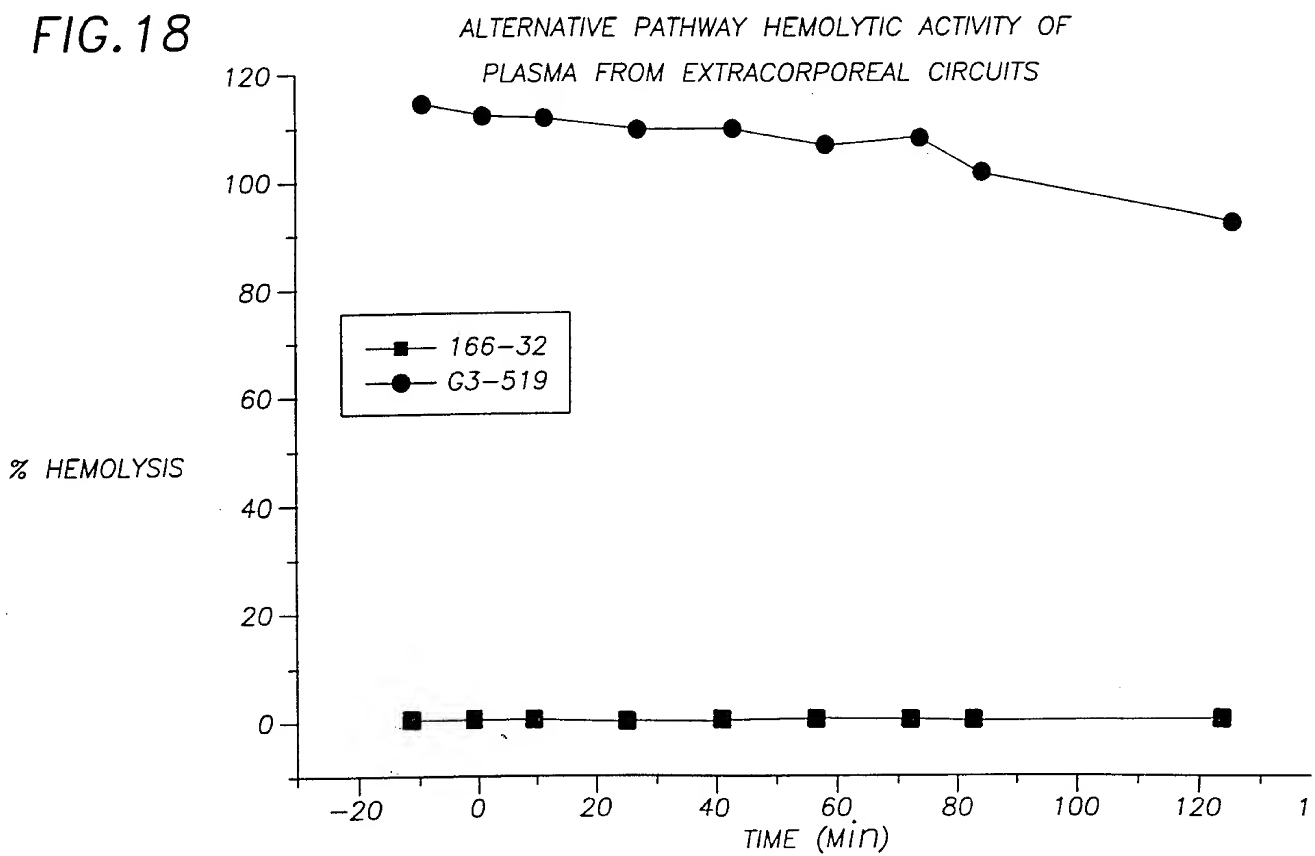
ALTERNATIVE PATHWAY HEMOLYTIC ACTIVITY OF
PLASMA FROM EXTRACORPOREAL CIRCUITS
% HEMOLYSIS
120
100
80
60
40
20
0
166-32
G3-519
-20
0
20
40
60
80
100
120
1
TIME (Min)

FIG. 19

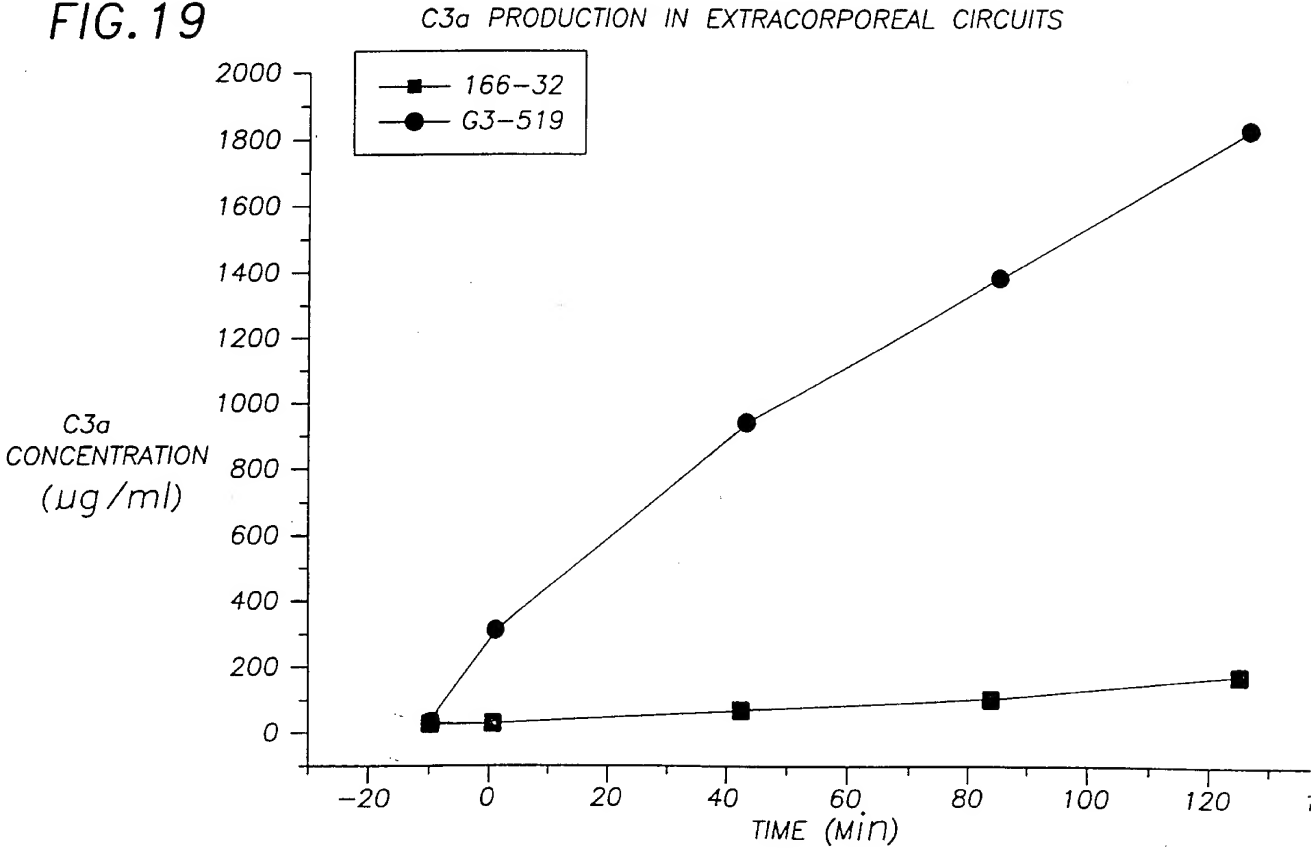
C3a PRODUCTION IN EXTRACORPOREAL CIRCUITS
166-32
G3-519
C3a CONCENTRATION (µg/ml)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-20
0
20
40
60
80
100
120
TIME (MIN)

FIG.20

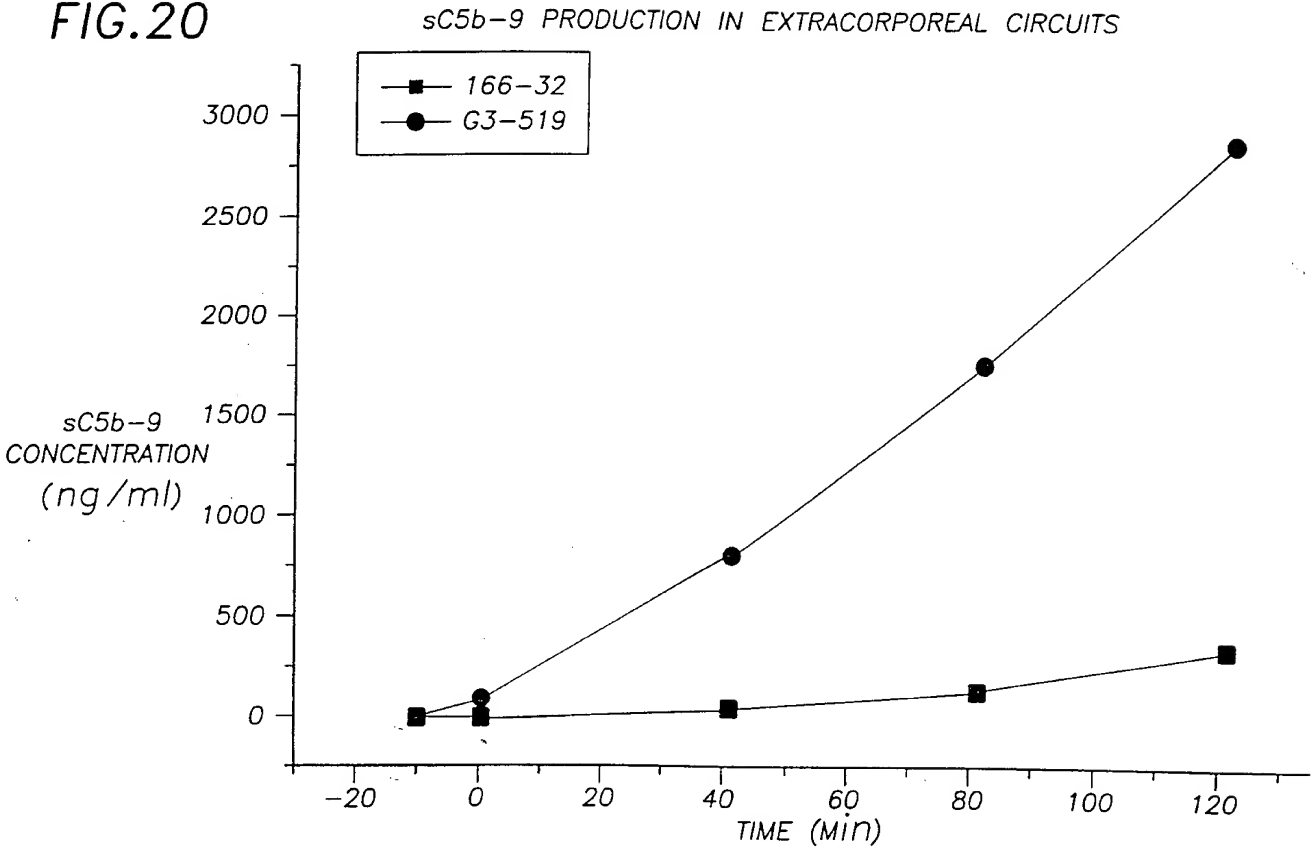

FIG.21

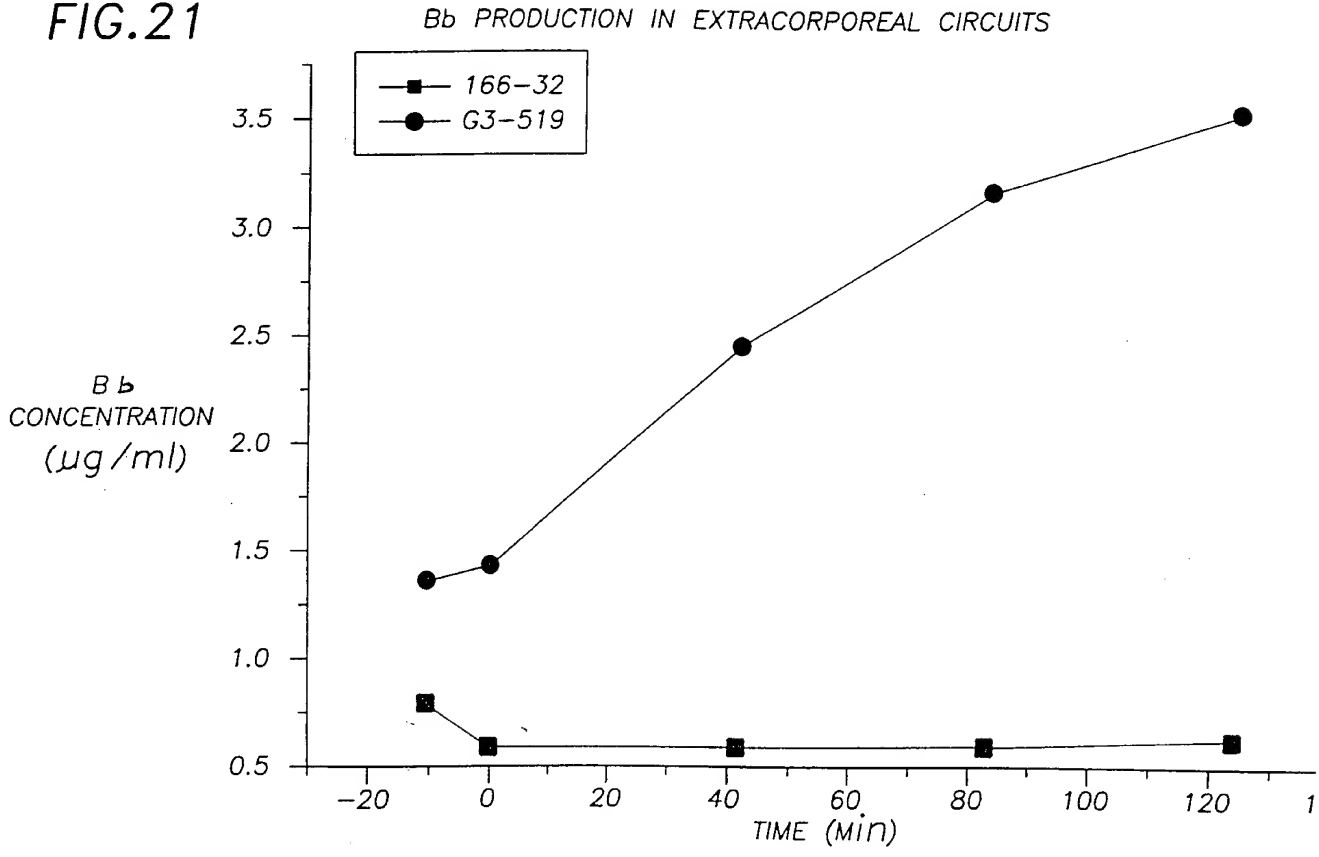
Bb PRODUCTION IN EXTRACORPOREAL CIRCUITS
166-32
G3-519
Bb CONCENTRATION (μg/ml)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
-20
0
20
40
60
80
100
120
TIME (Min)

FIG.22

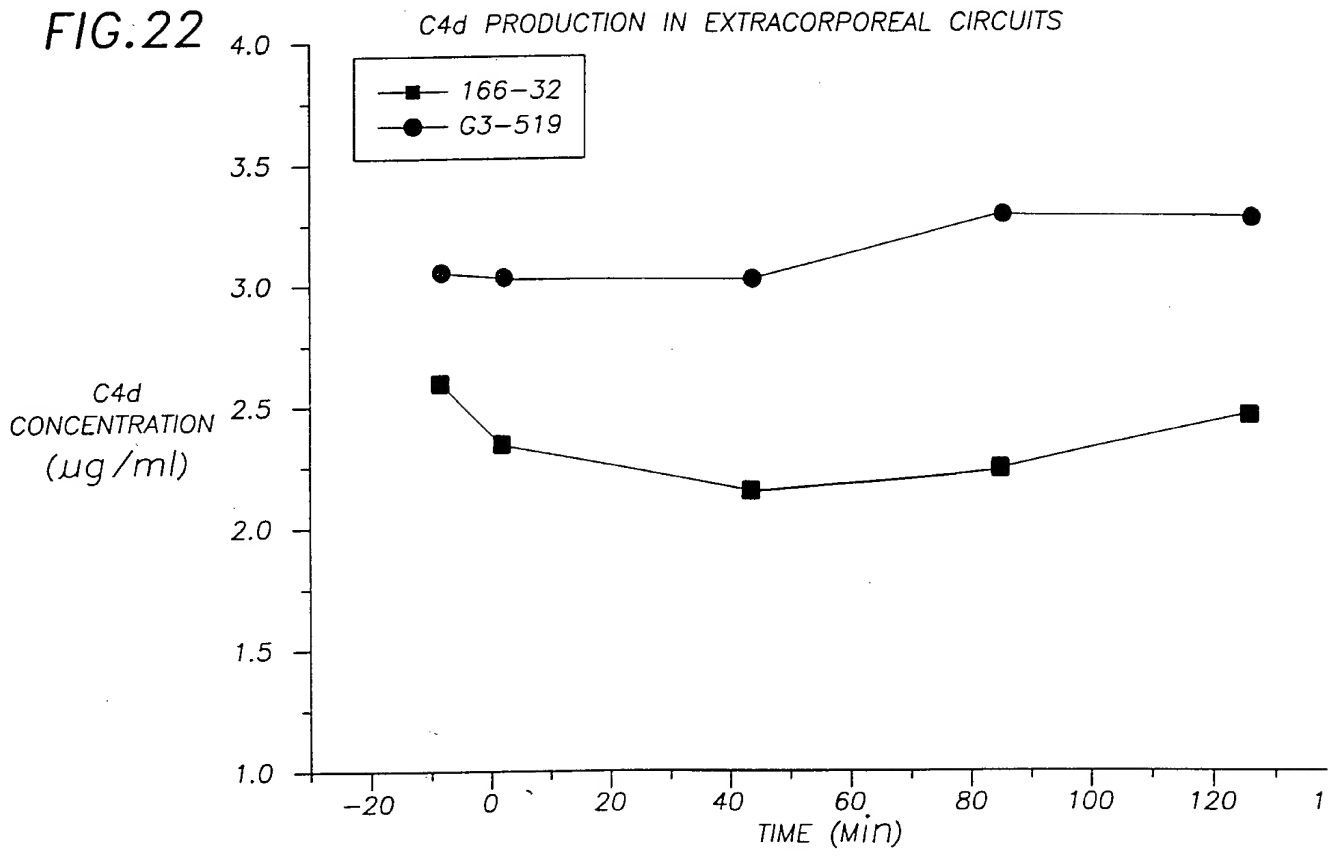
C4d PRODUCTION IN EXTRACORPOREAL CIRCUITS
166-32
G3-519
C4d CONCENTRATION (μg/ml)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
-20
0
20
40
60
80
100
120
TIME (MIN)

FIG.23

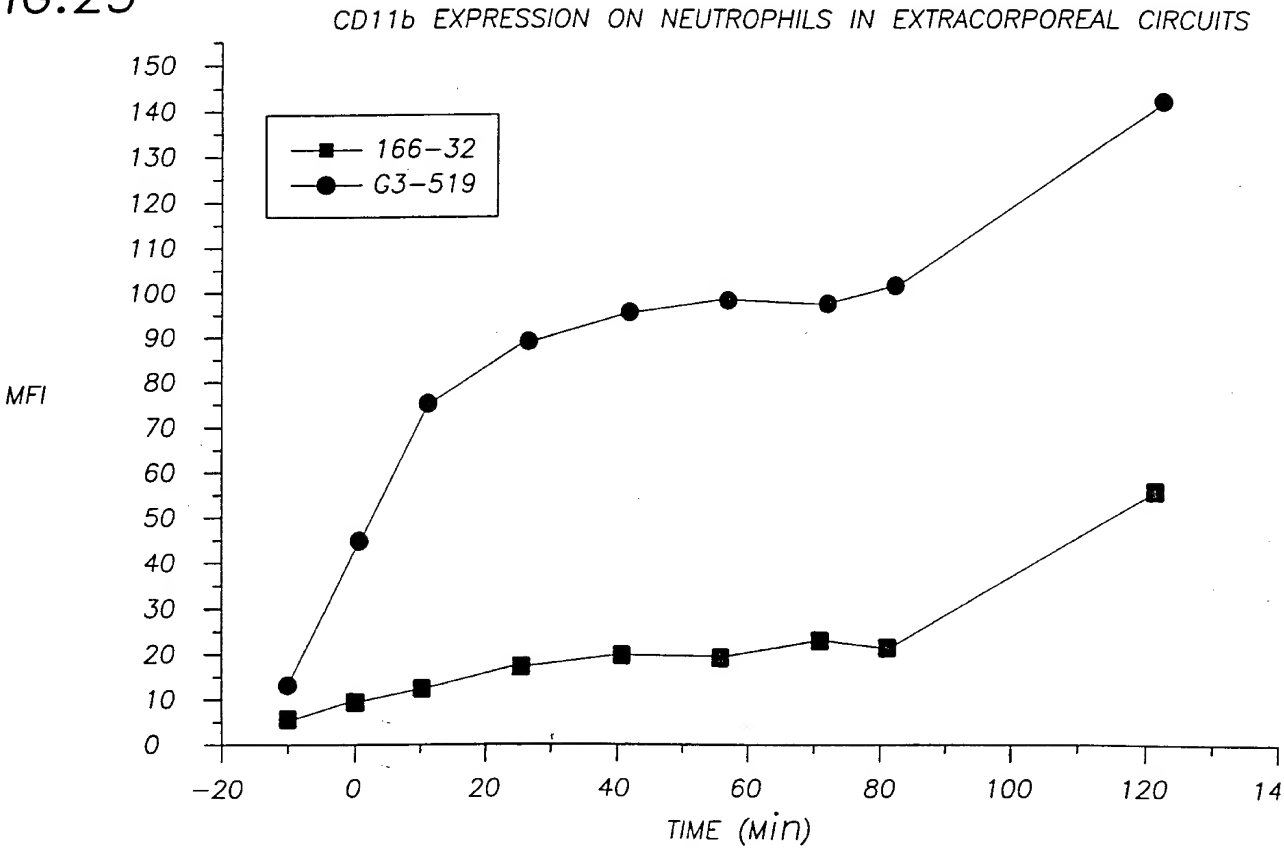
CD11b EXPRESSION ON NEUTROPHILS IN EXTRACORPOREAL CIRCUITS
166-32
G3-519
MFI
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-20
0
20
40
60
80
100
120
14
TIME (min)

FIG.24

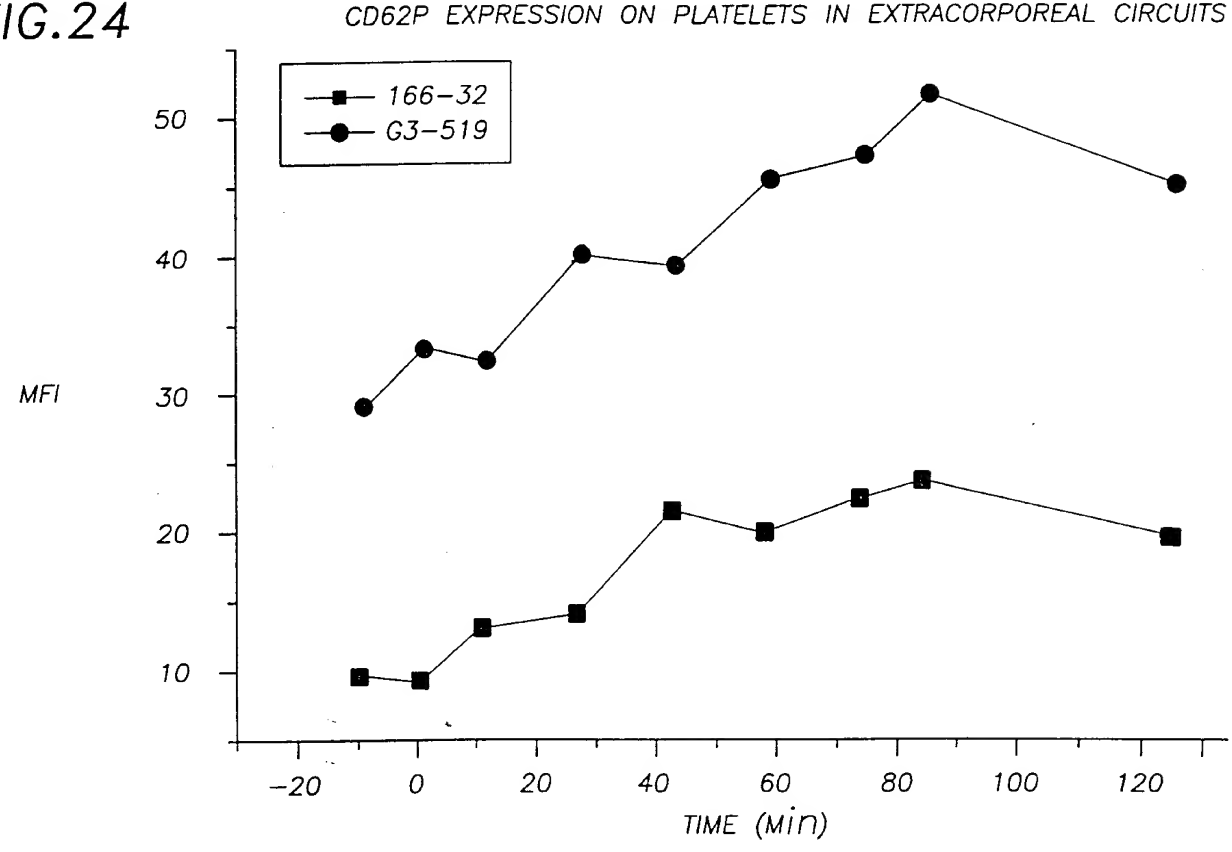
CD62P EXPRESSION ON PLATELETS IN EXTRACORPOREAL CIRCUITS
166-32
G3-519
MFI
50
40
30
20
10
-20
0
20
40
60
80
100
120
TIME (MIN)

FIG.25

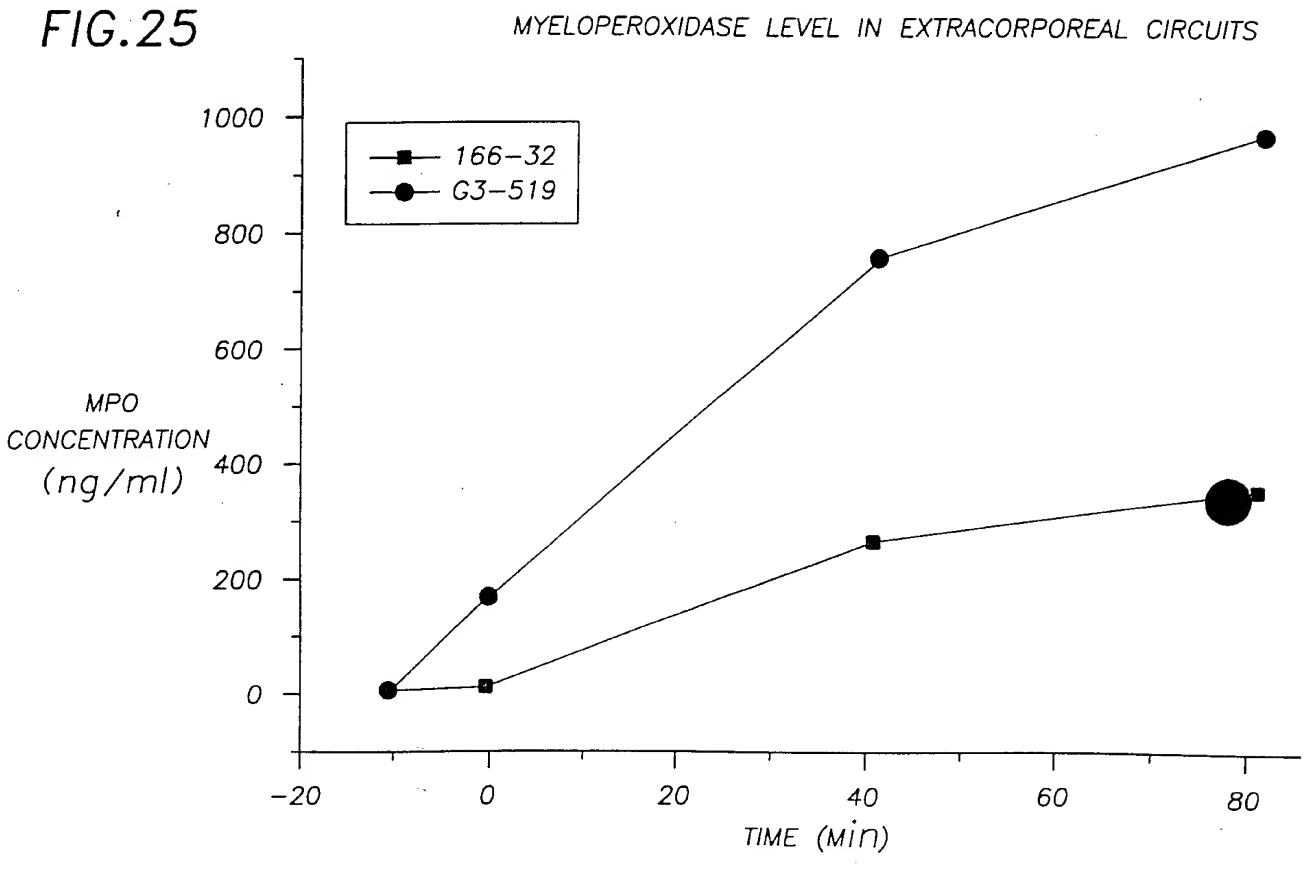
MYELOPEROXIDASE LEVEL IN EXTRACORPOREAL CIRCUITS
166-32
G3-519
MPO CONCENTRATION (ng/ml)
1000
800
600
400
200
0
-20
0
20
40
60
80
TIME (MIN)

Fig. 26 Selective inhibition of the alternative complement pathway by anti-factor D MAb 166-32

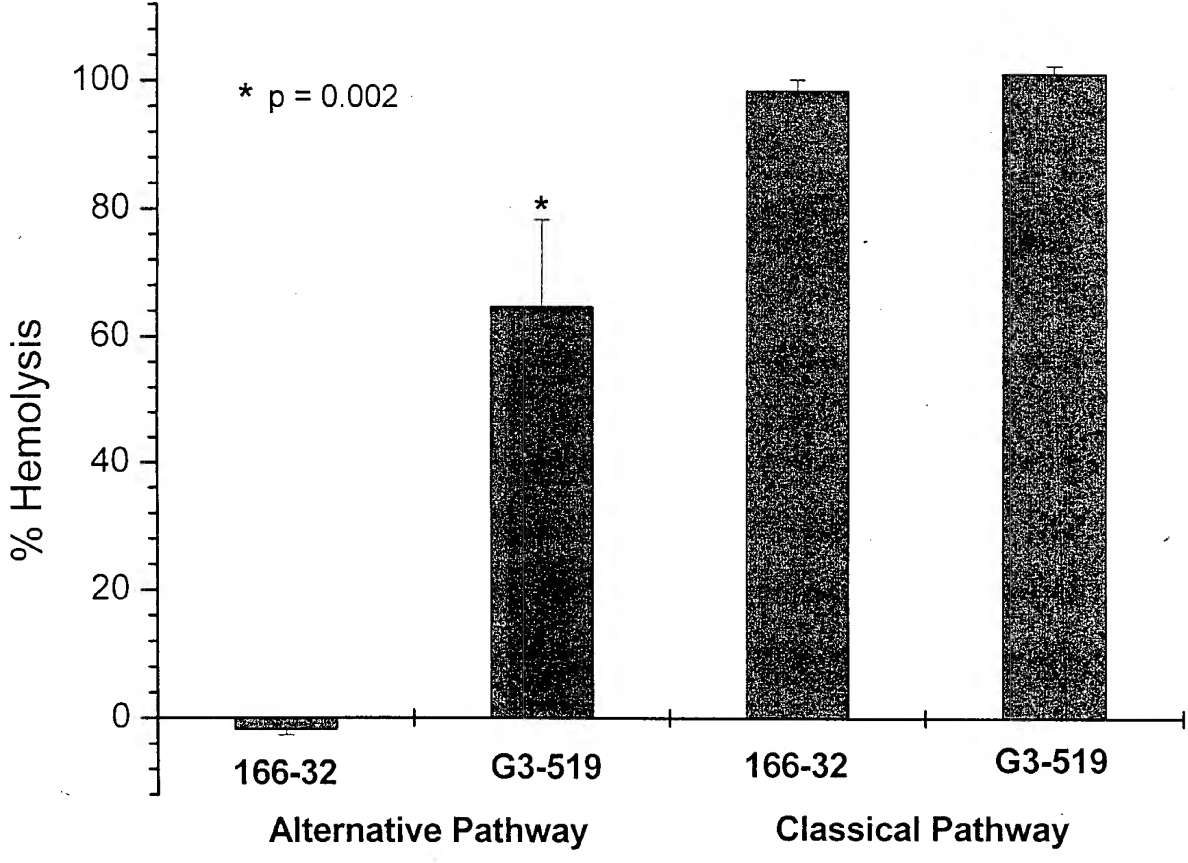

Fig. 27 Bb production in extracorporeal circuits

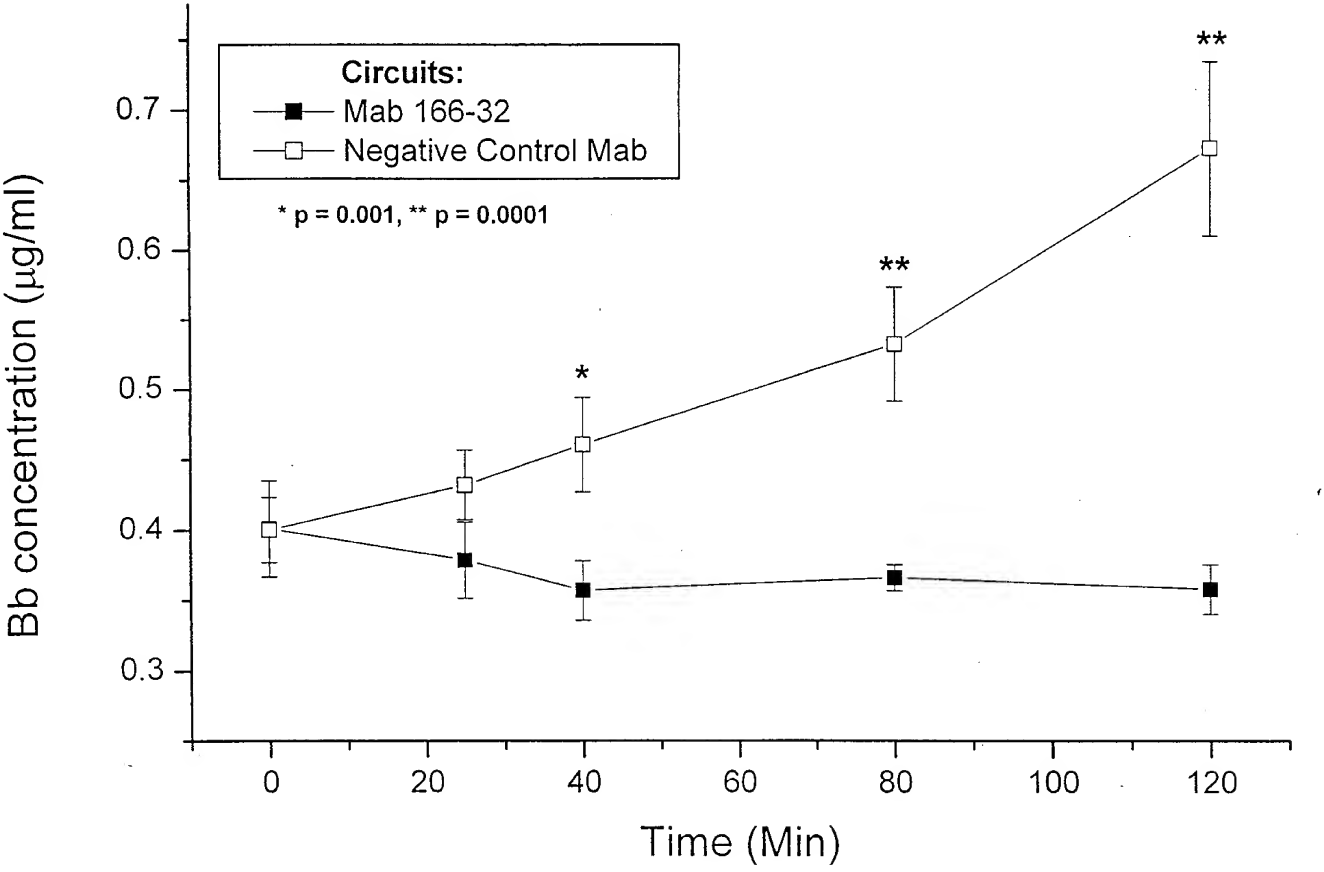

Fig. 28 C4d production in extracorporeal circuits

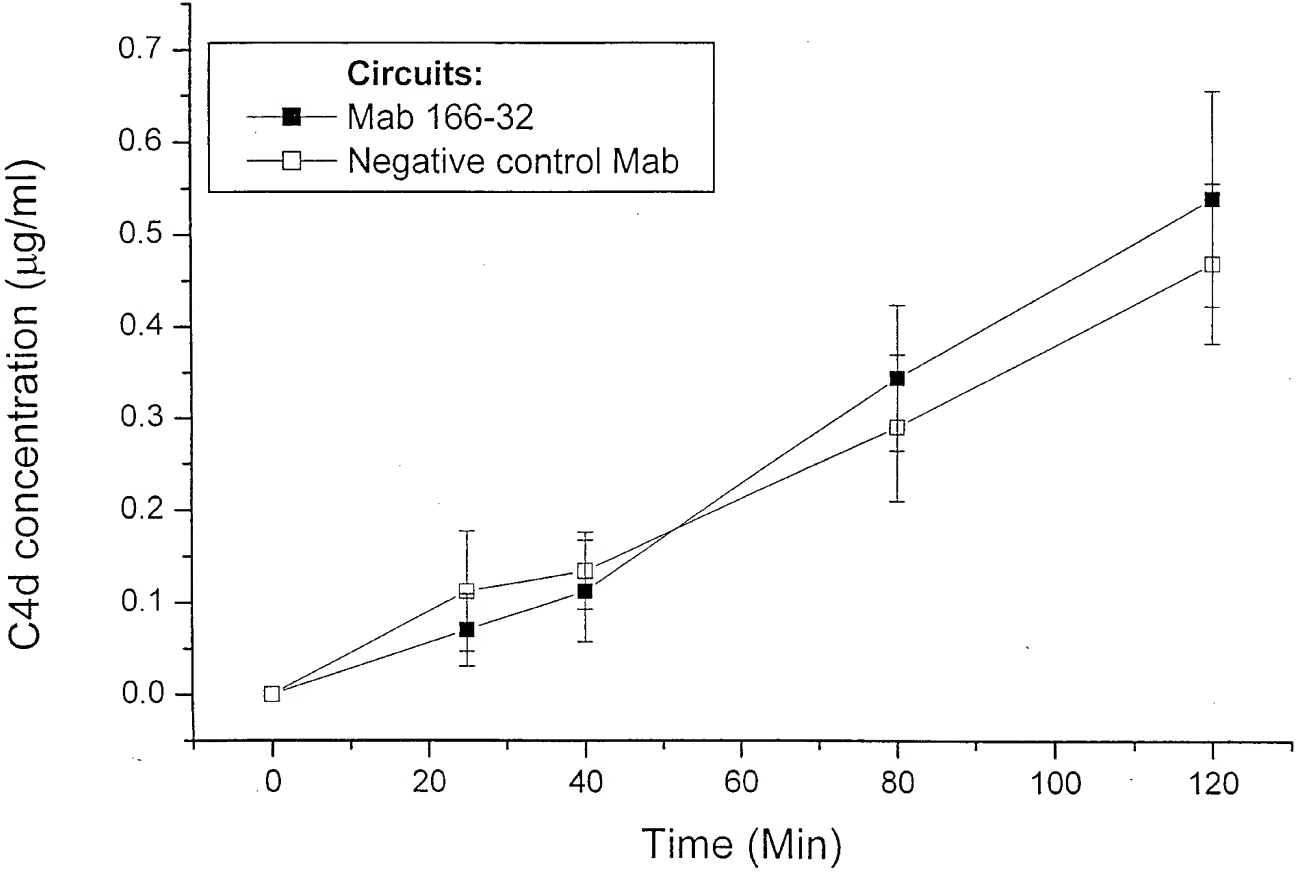

Fig. 29 C3a production in extracorporeal circuits

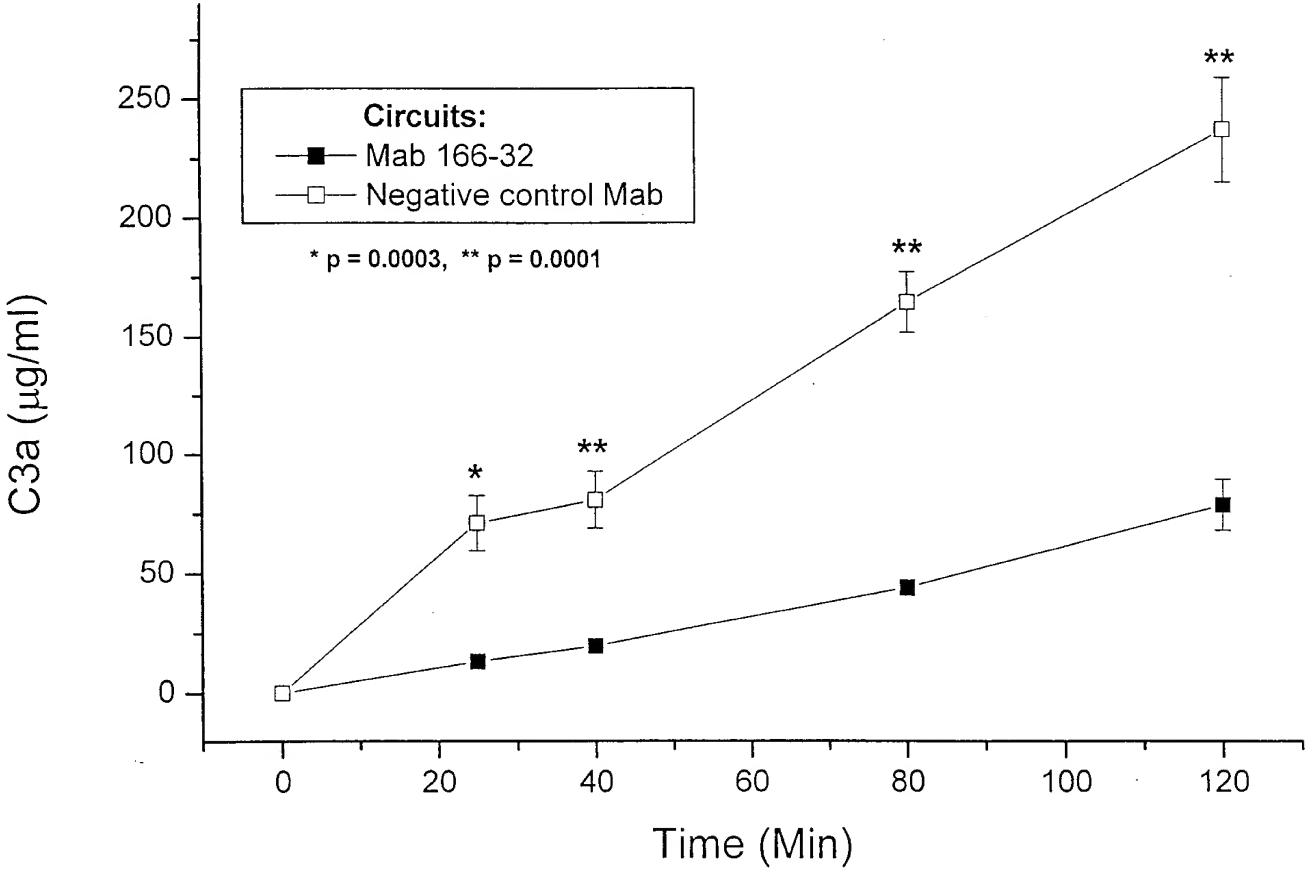

Fig. 30 sC5b-9 production in extracorporeal circuits

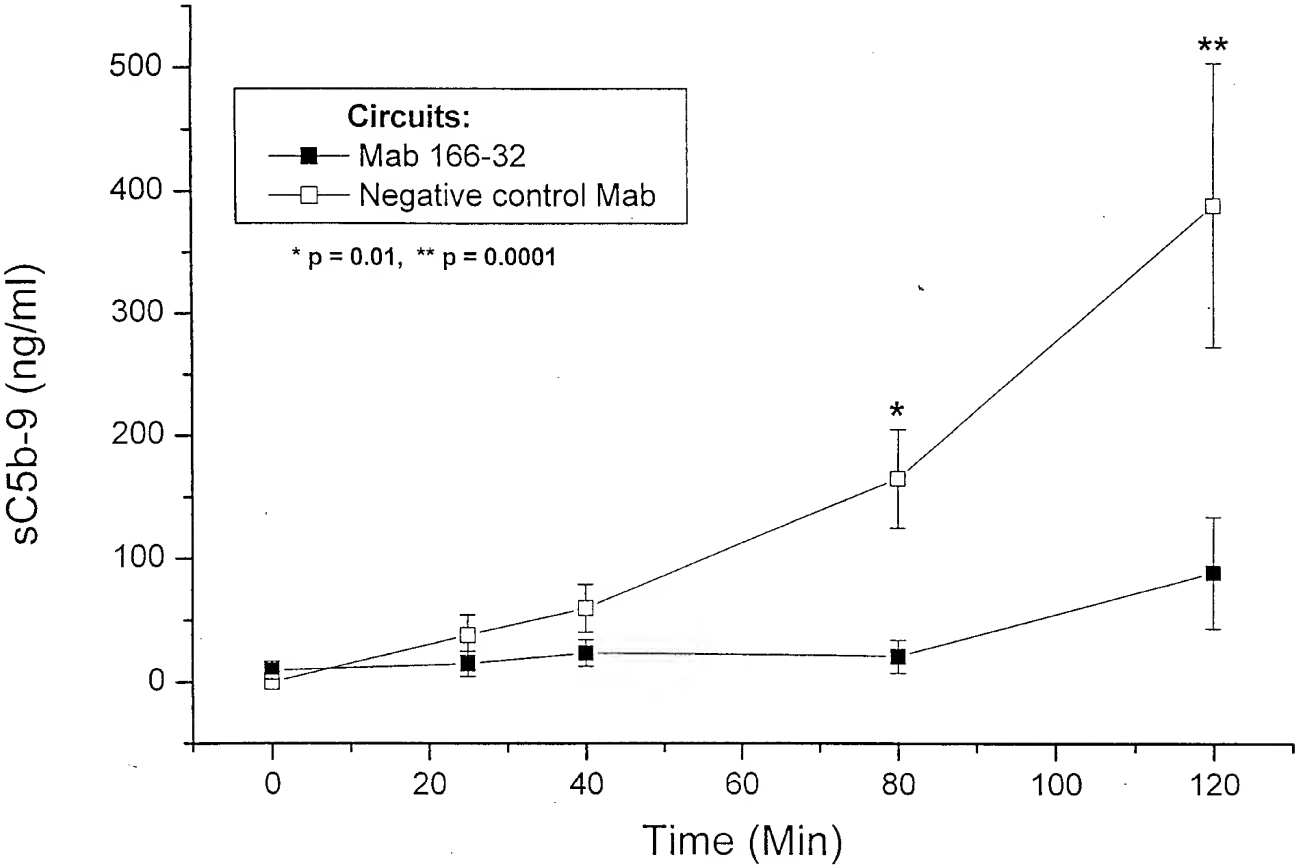

Fig. 31 C5a production in extracorporeal circuits

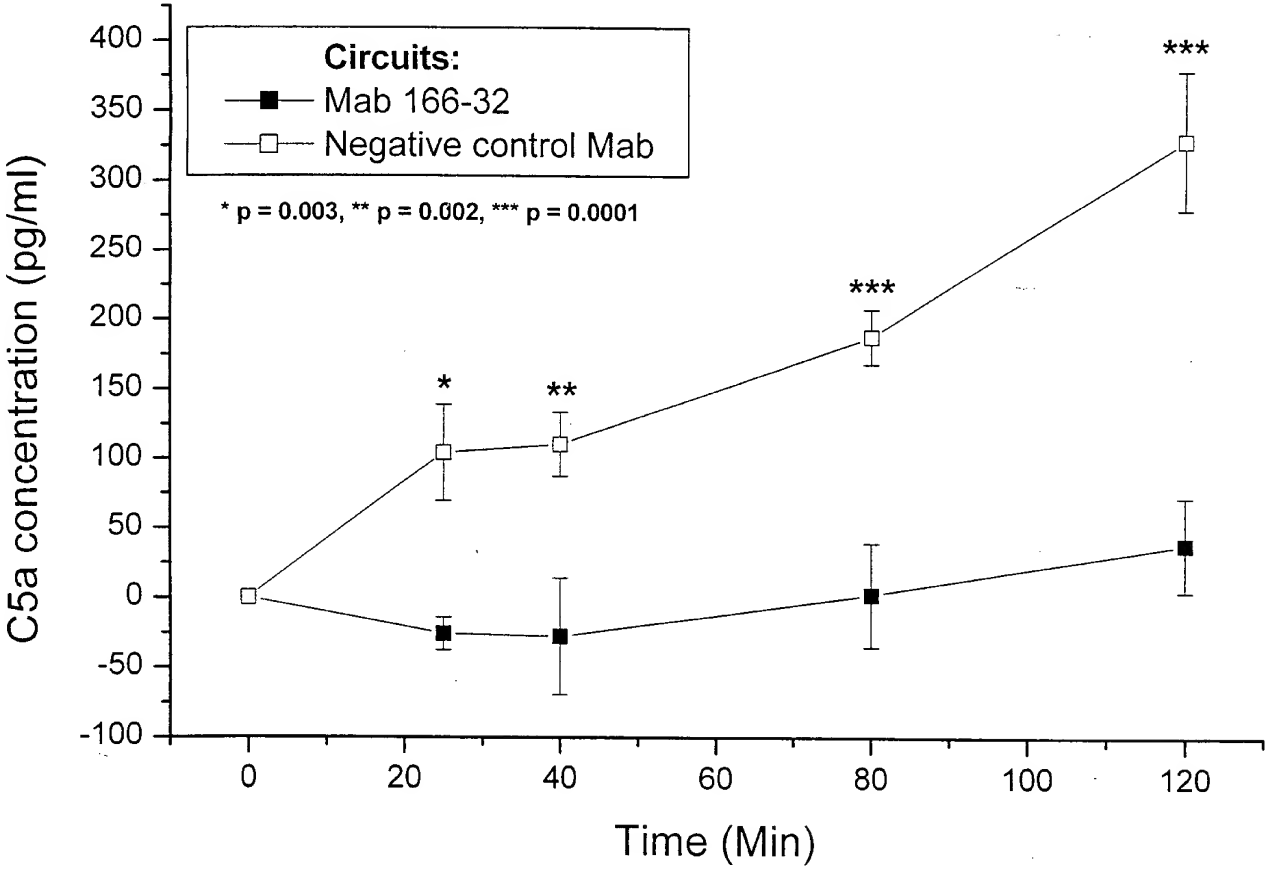

Fig. 32 CD11b expression on neutrophils in extracorporeal circuits

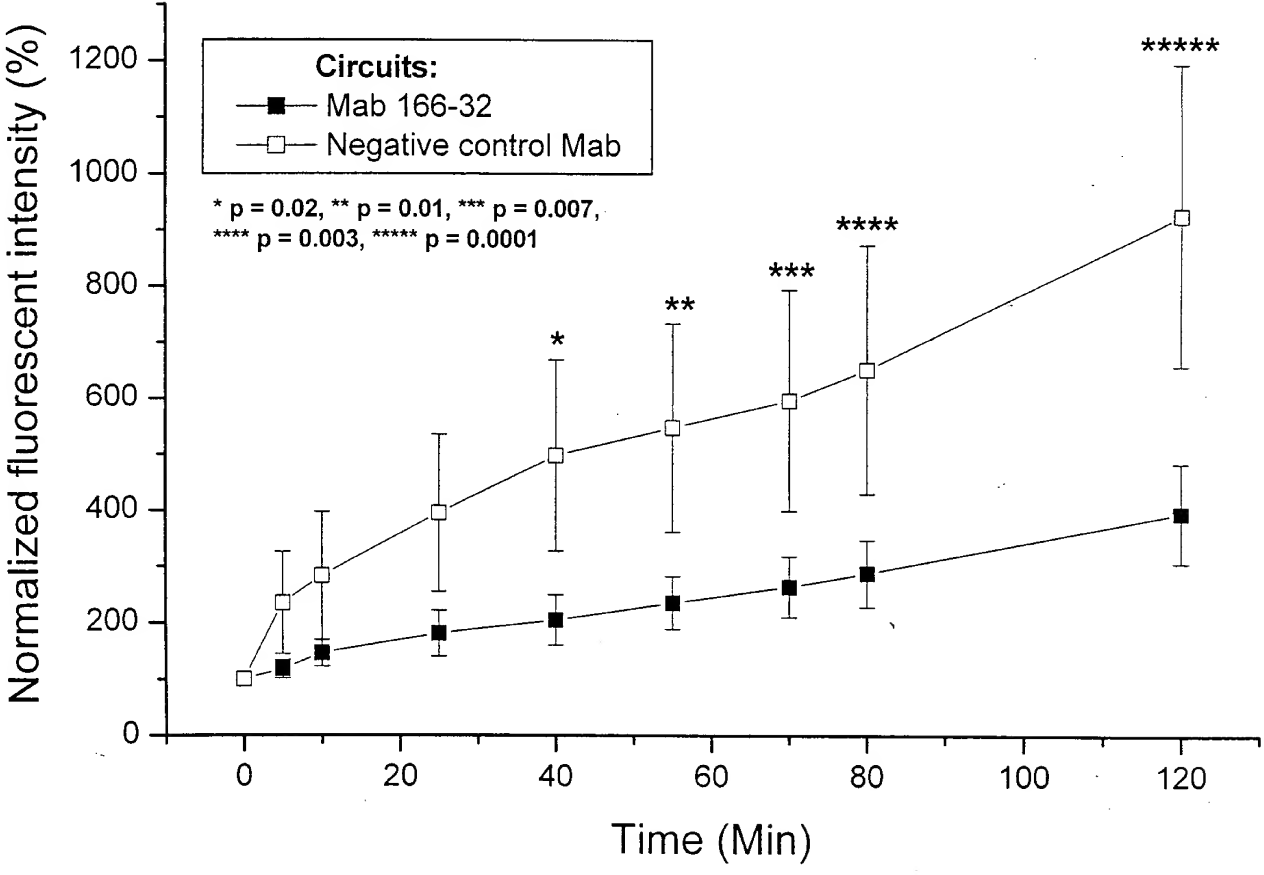

Fig. 33 Myeloperoxidase production in extracorporeal circuits

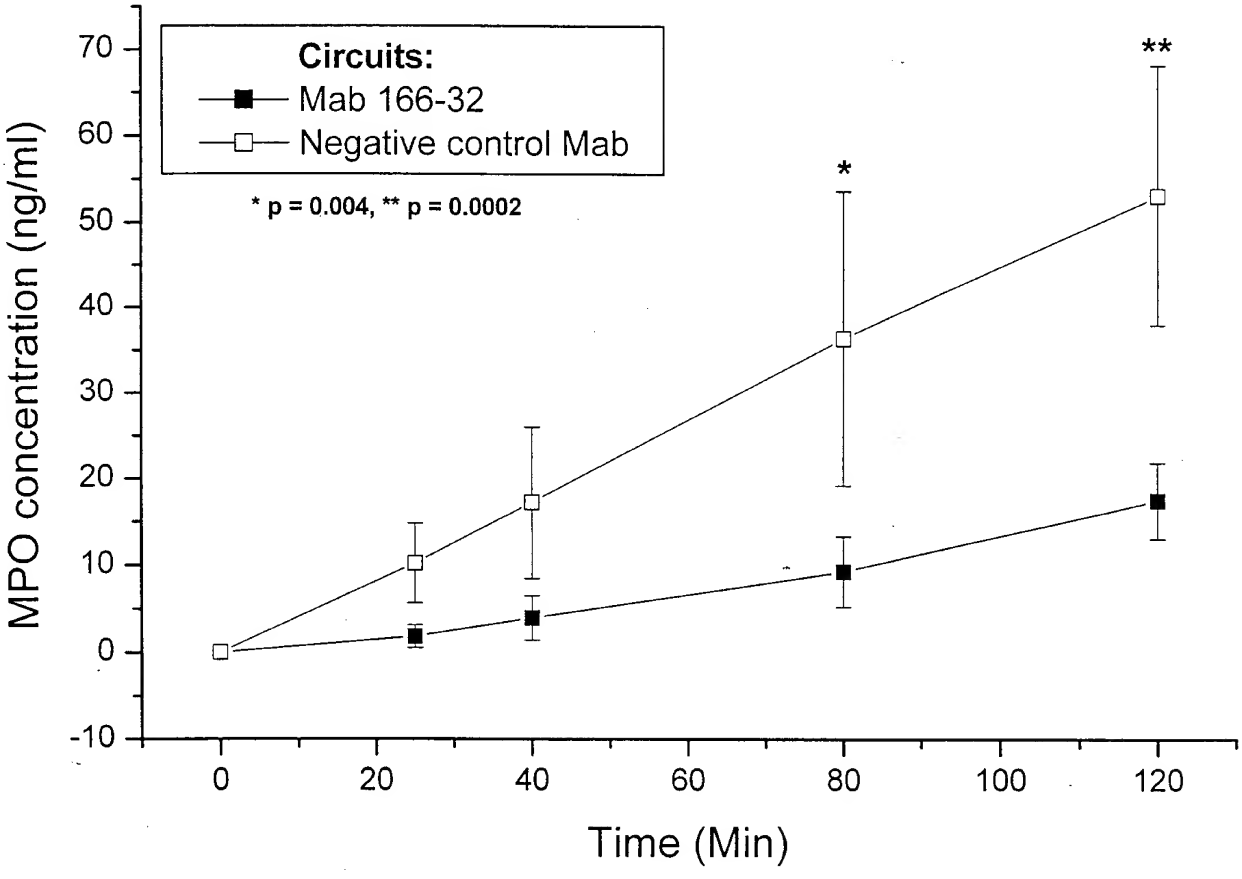

Fig. 34 Elastase-α1-antitrypsin production in extracorporeal circuits

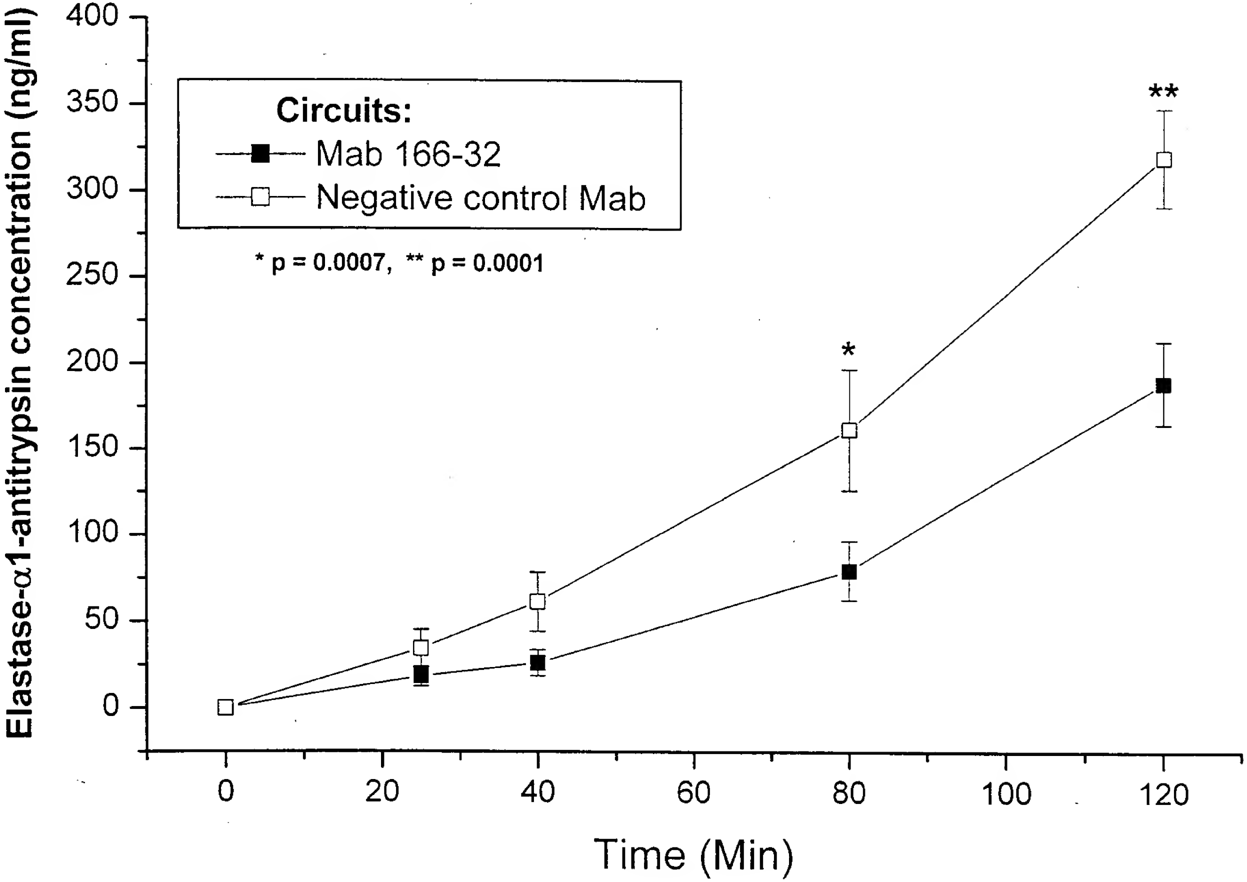

Fig. 35 CD62P expression on platelets in extracorporeal circuits

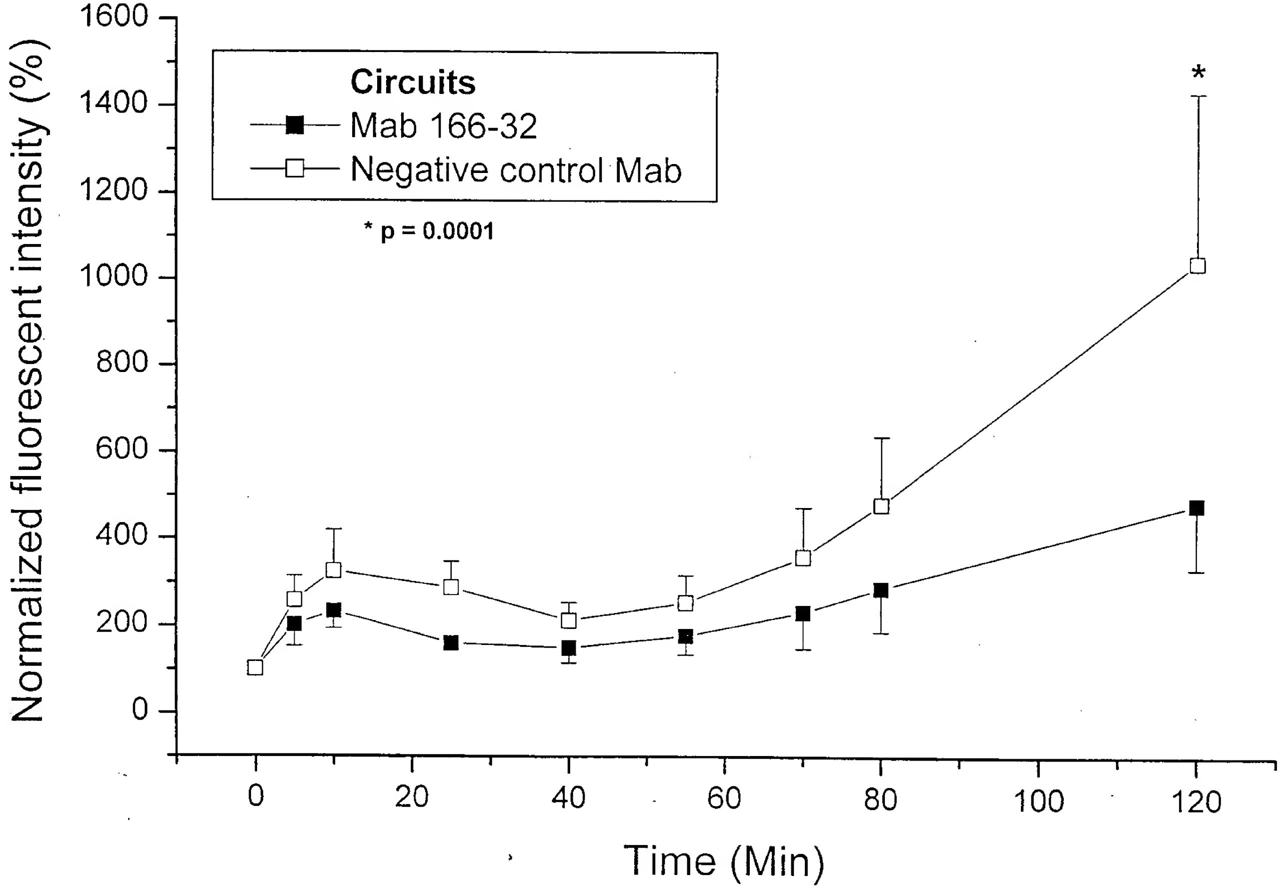

Fig. 36 CD62P-positive platelets in extracorporeal circuits

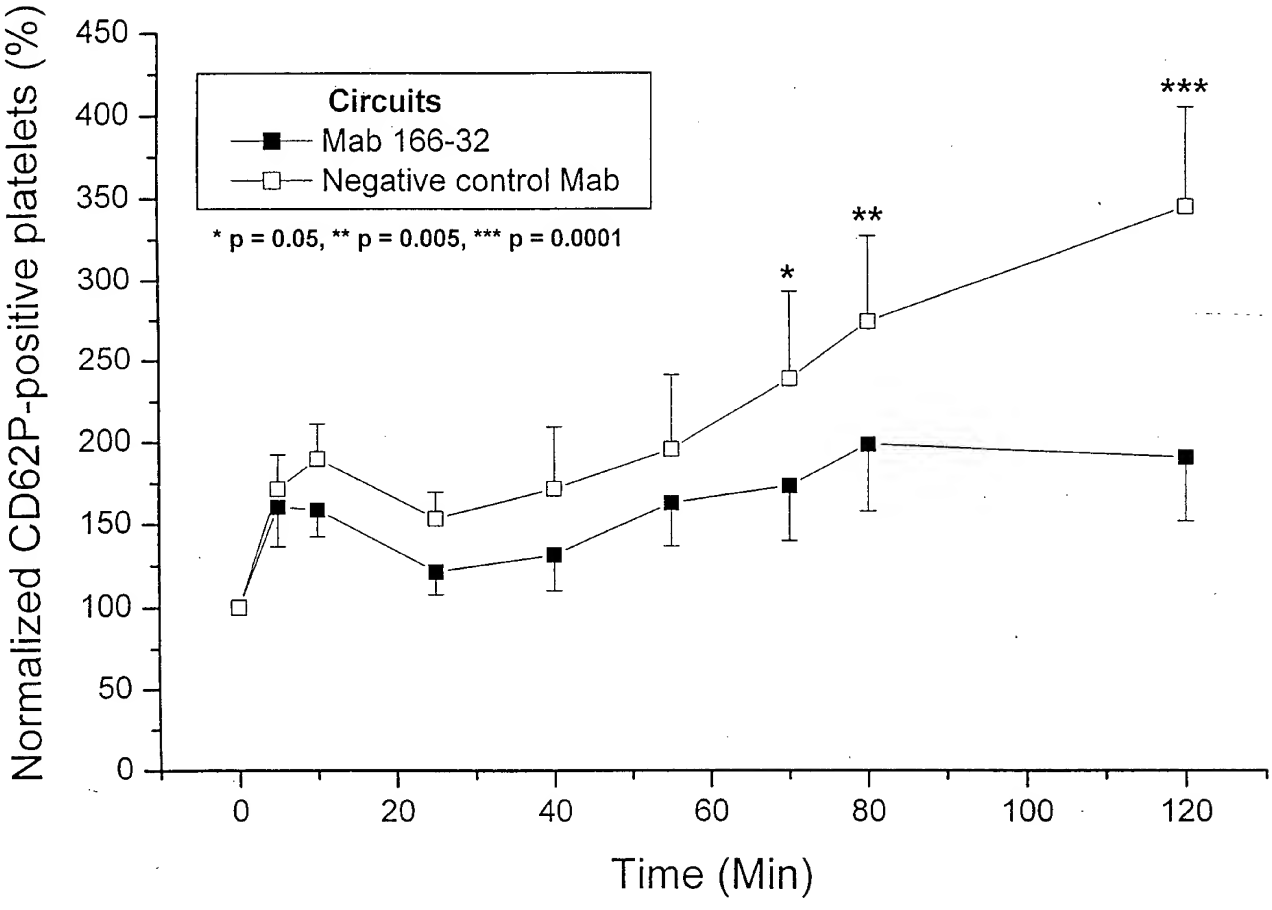

Fig. 37 Platelet thrombospondin production in extracorporeal circuits

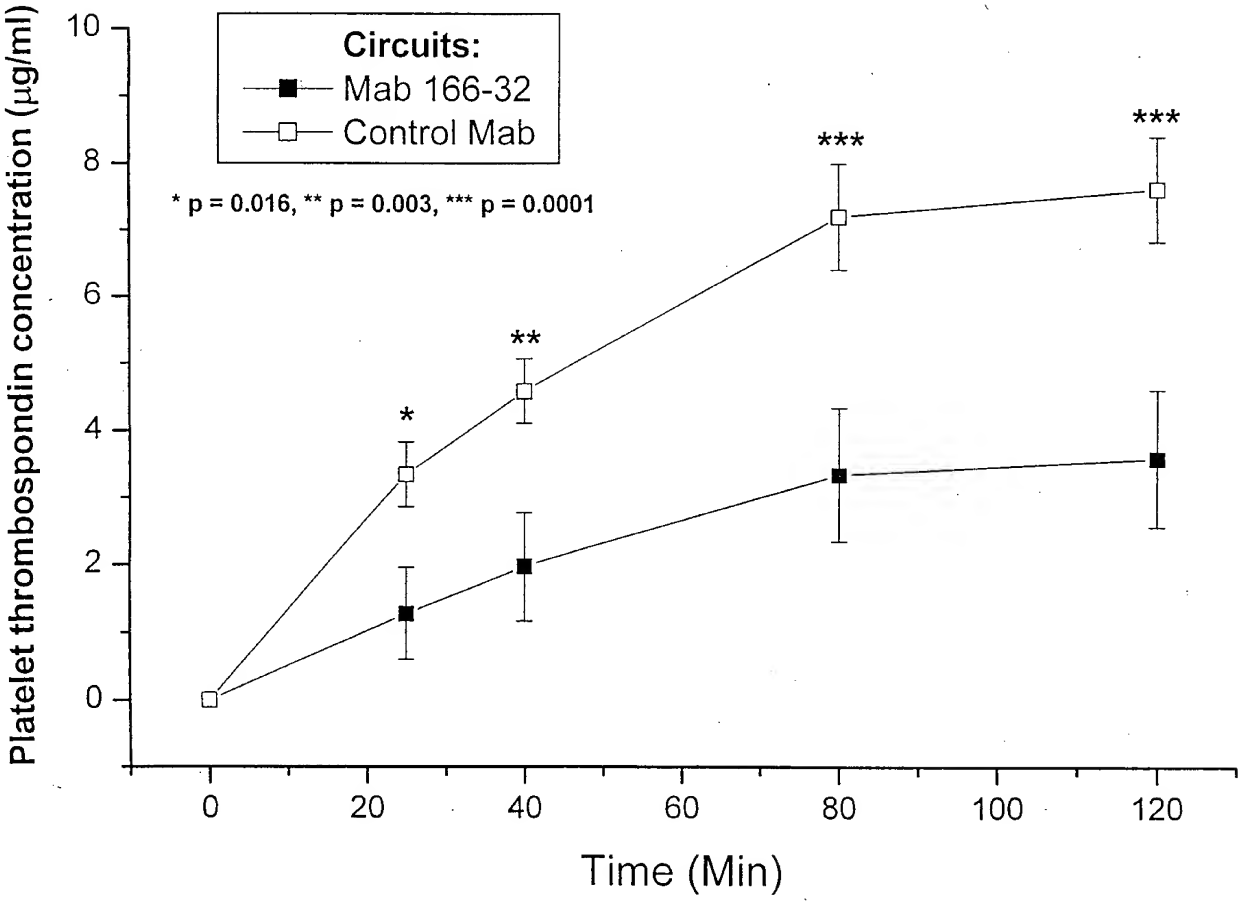

Fig. 38 IL-8 production in extracorporeal circuits

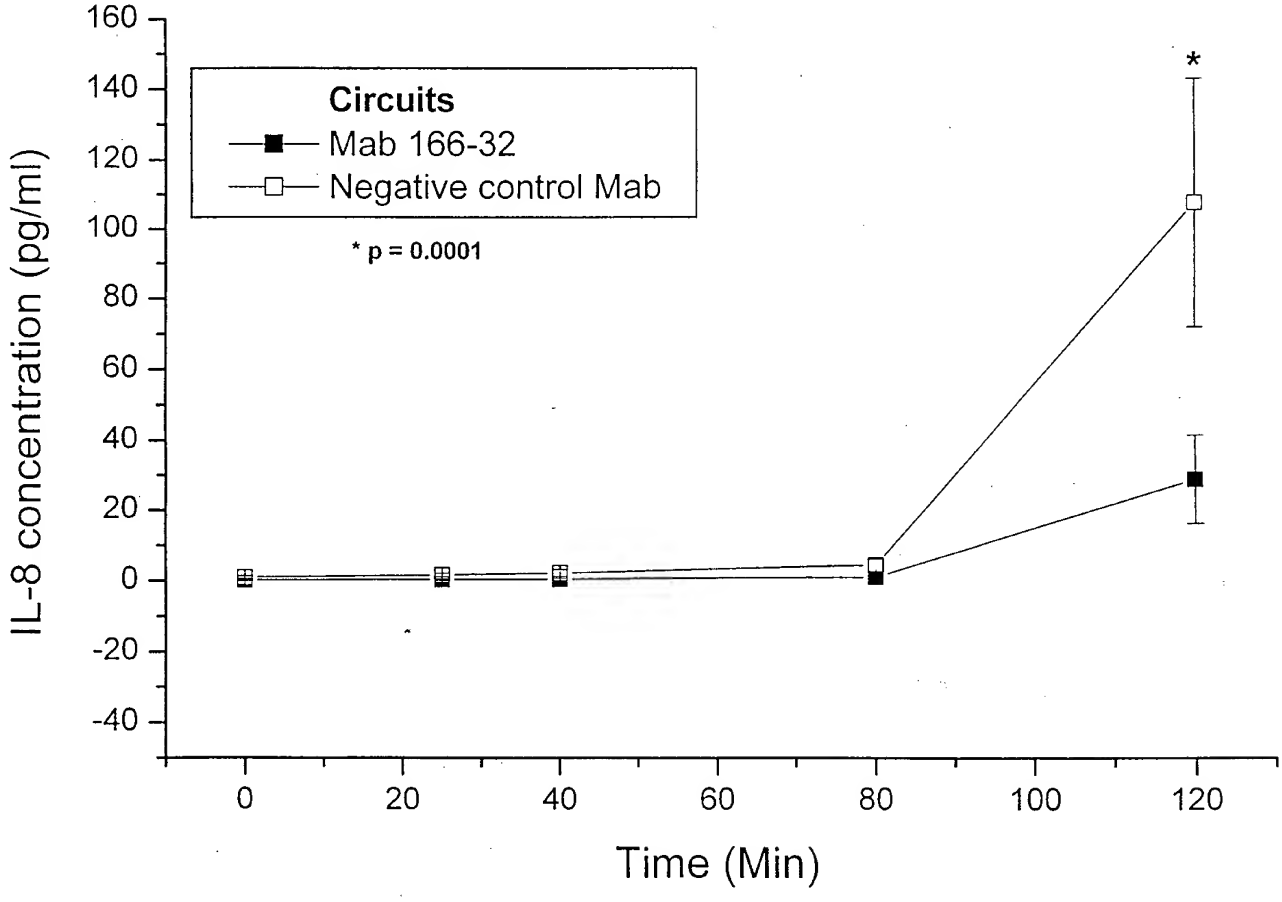

Fig. 39 Pharmacokinetics of MAb166-32 in Baboon CPB

(5 mg/kg MAb166-32, single iv. bolus)

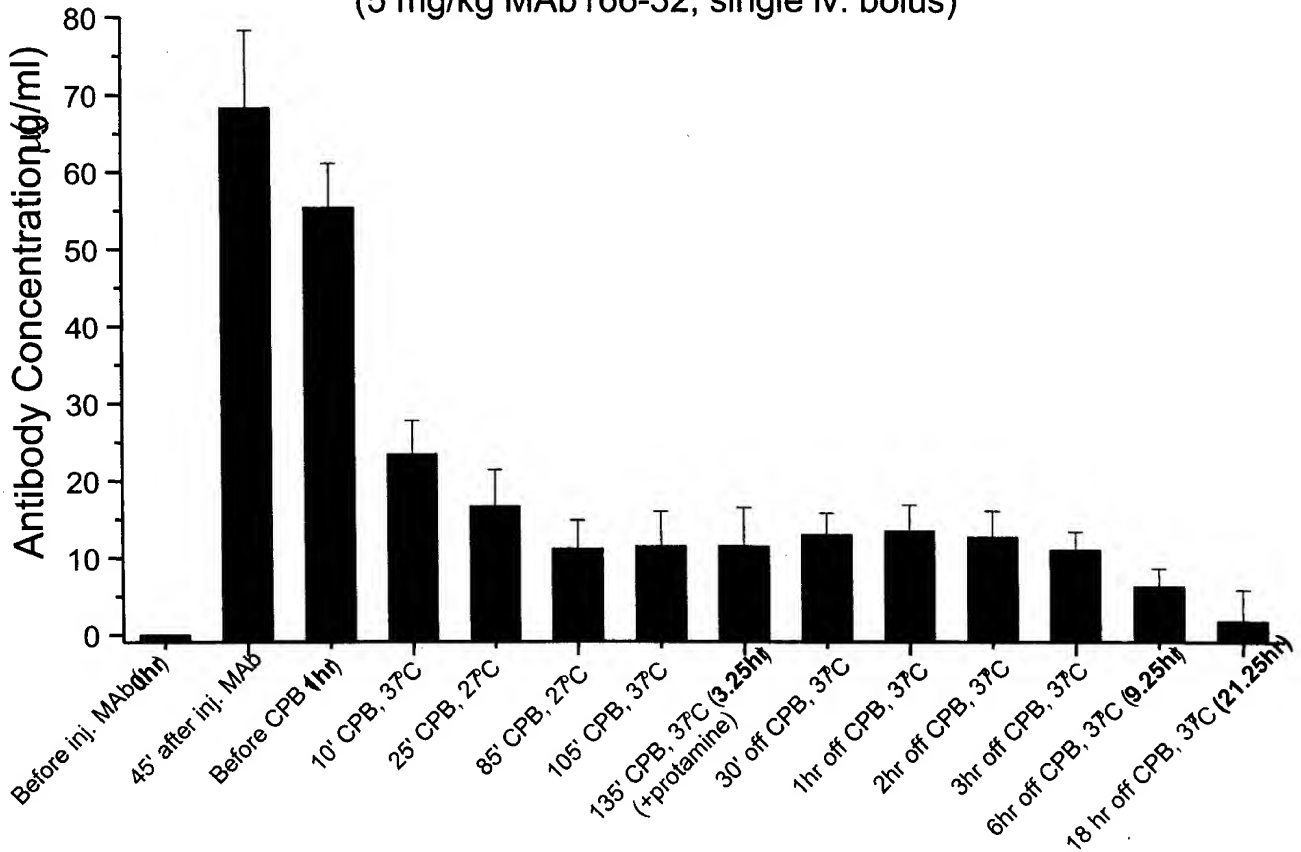

Fig. 40 Inhibition of Alternative Complement by MAb166-32 in Baboon CPB

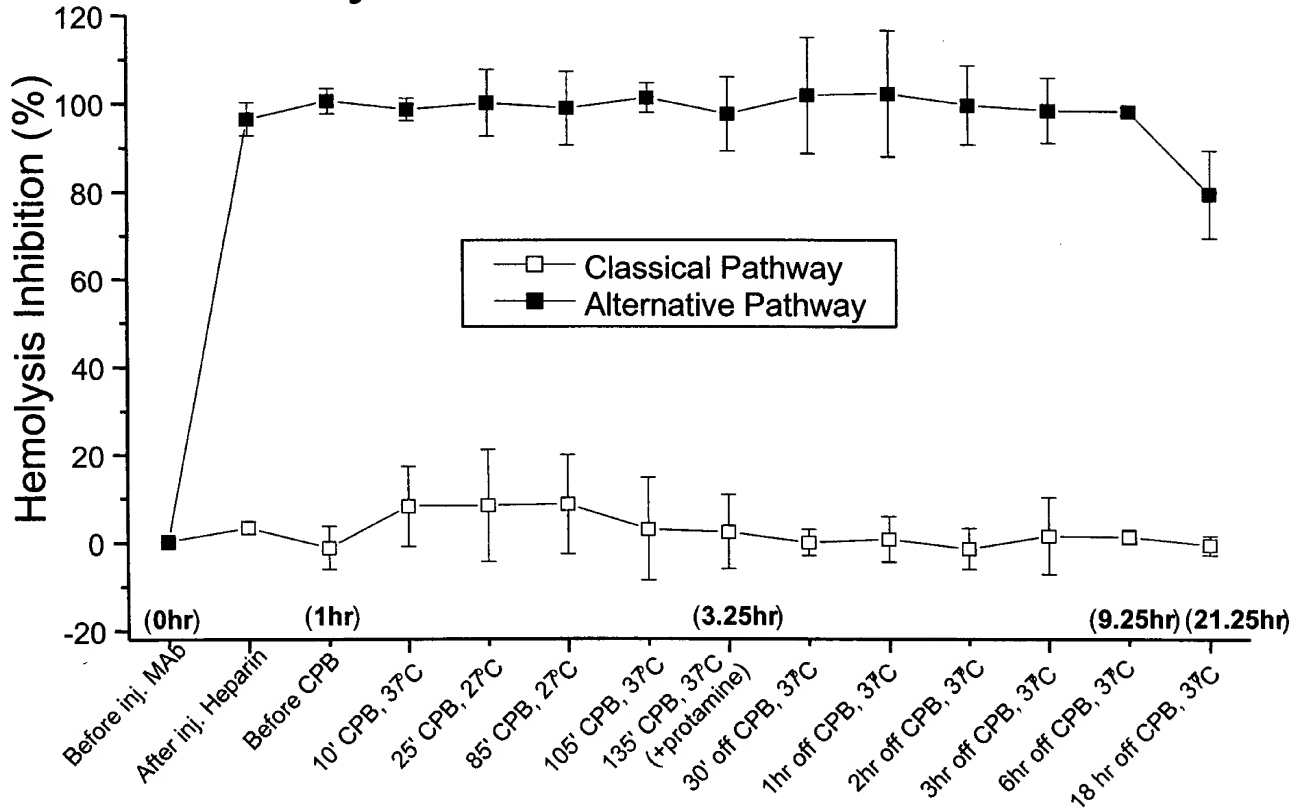

Fig. 41 Bb in Baboon CPB

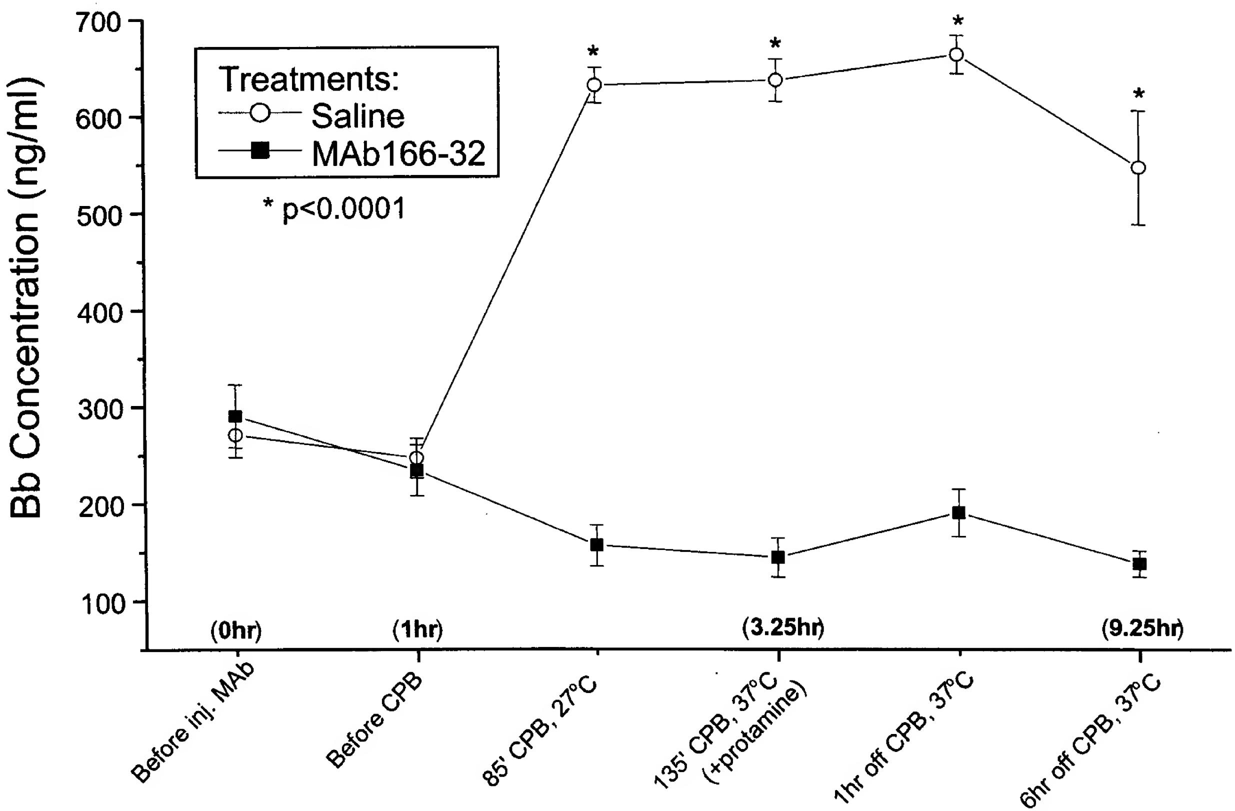

Fig. 42 C4d in Baboon CPB

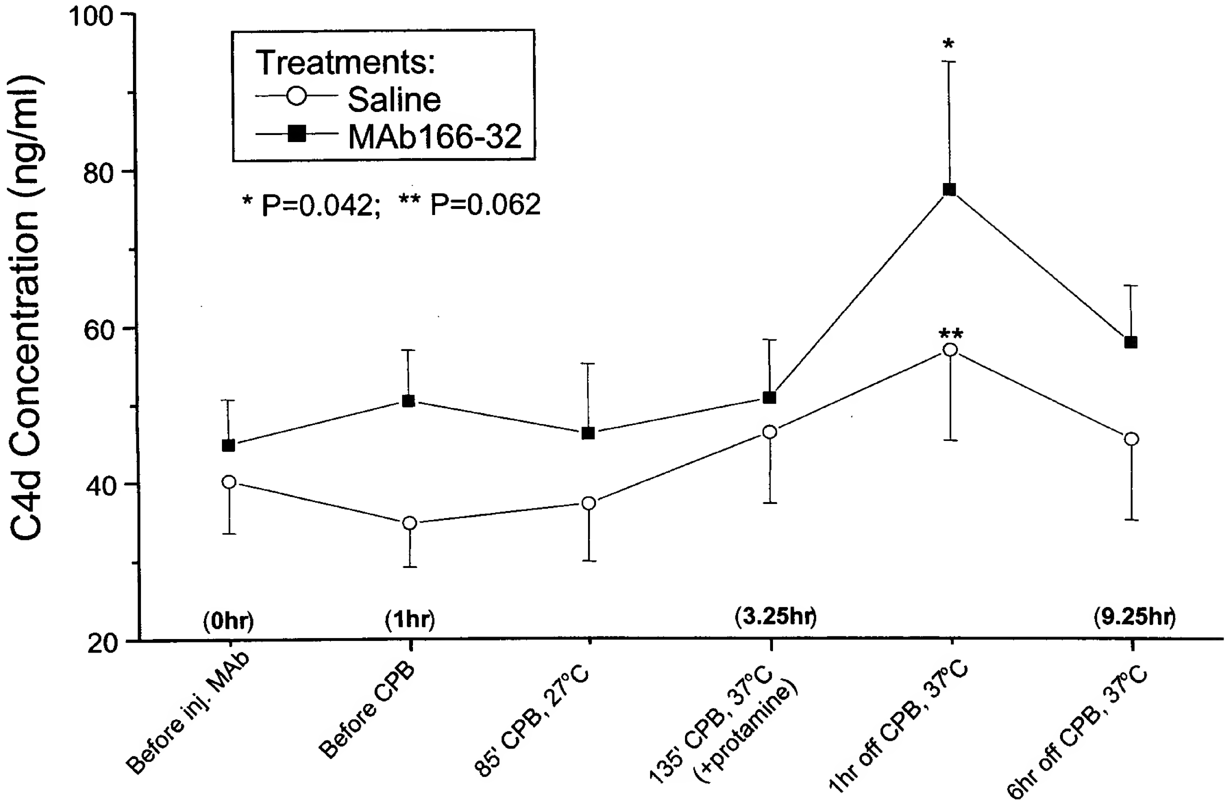

Fig. 43 C3a in Baboon CPB

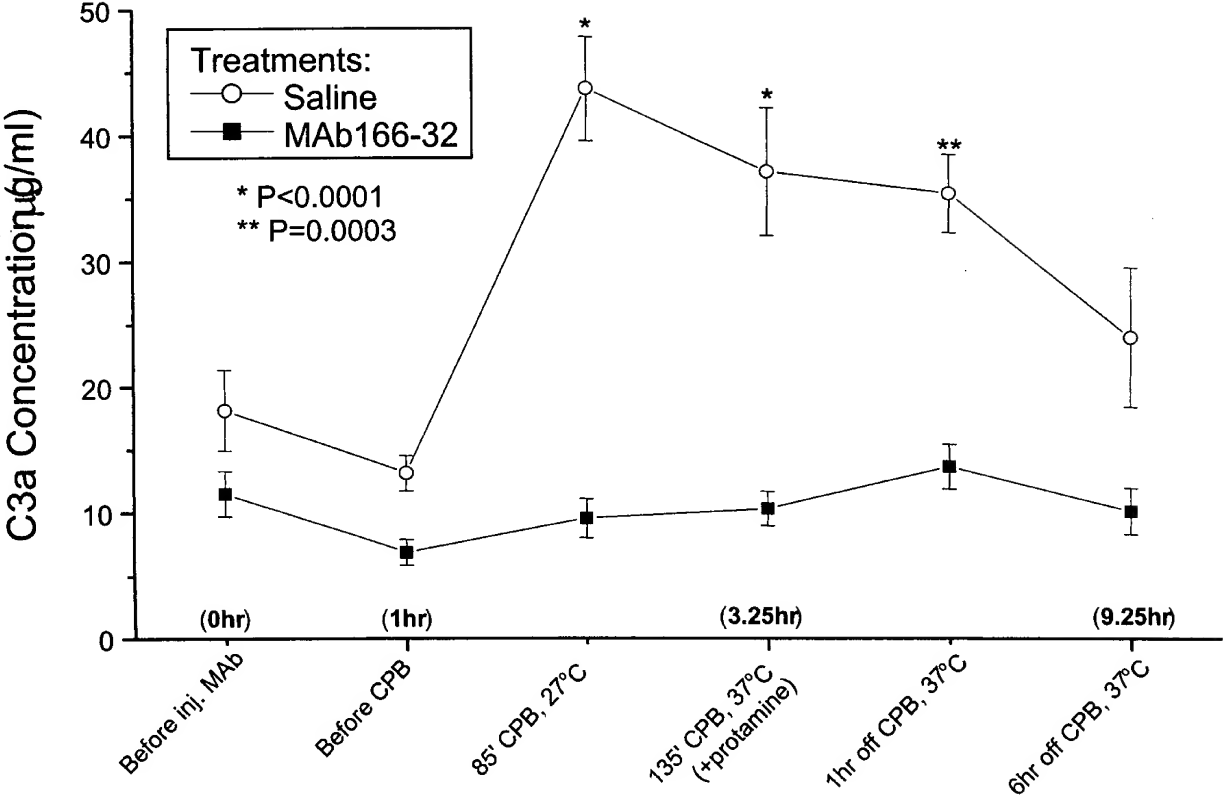

Fig. 44 CD11b Expression on Neutrophils in Baboon CPB

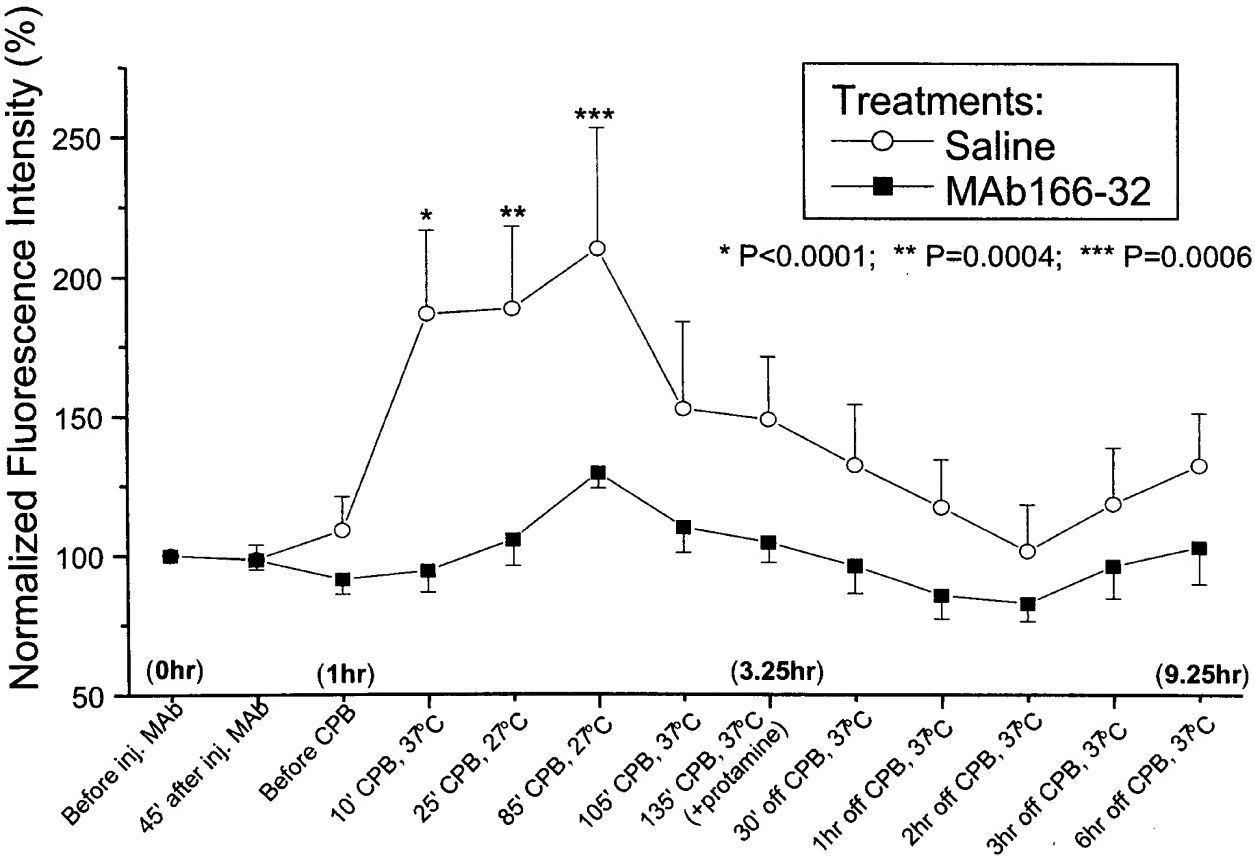

Fig. 45 CD11b Expression on Monocytes in Baboon CPB

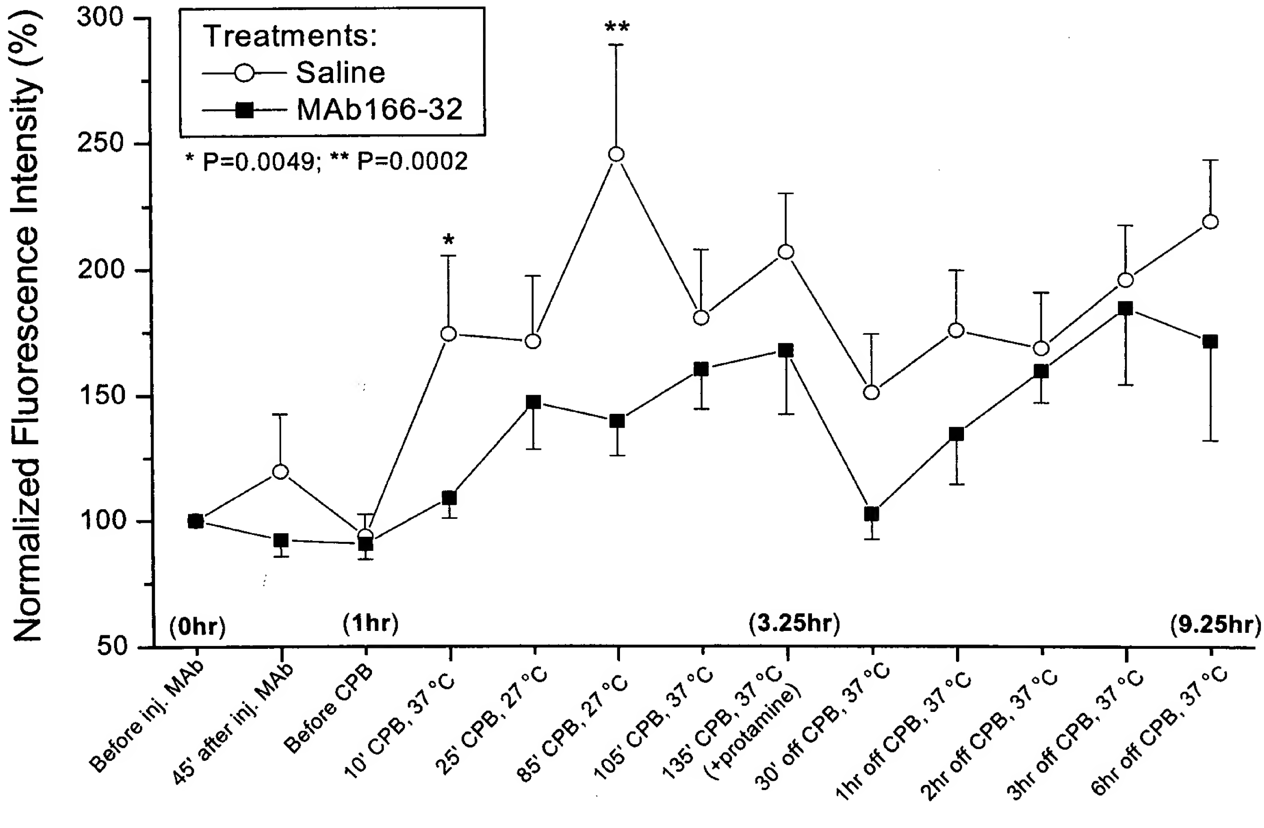

Fig. 4b CD62P Expression on Platelets in Baboon CPB

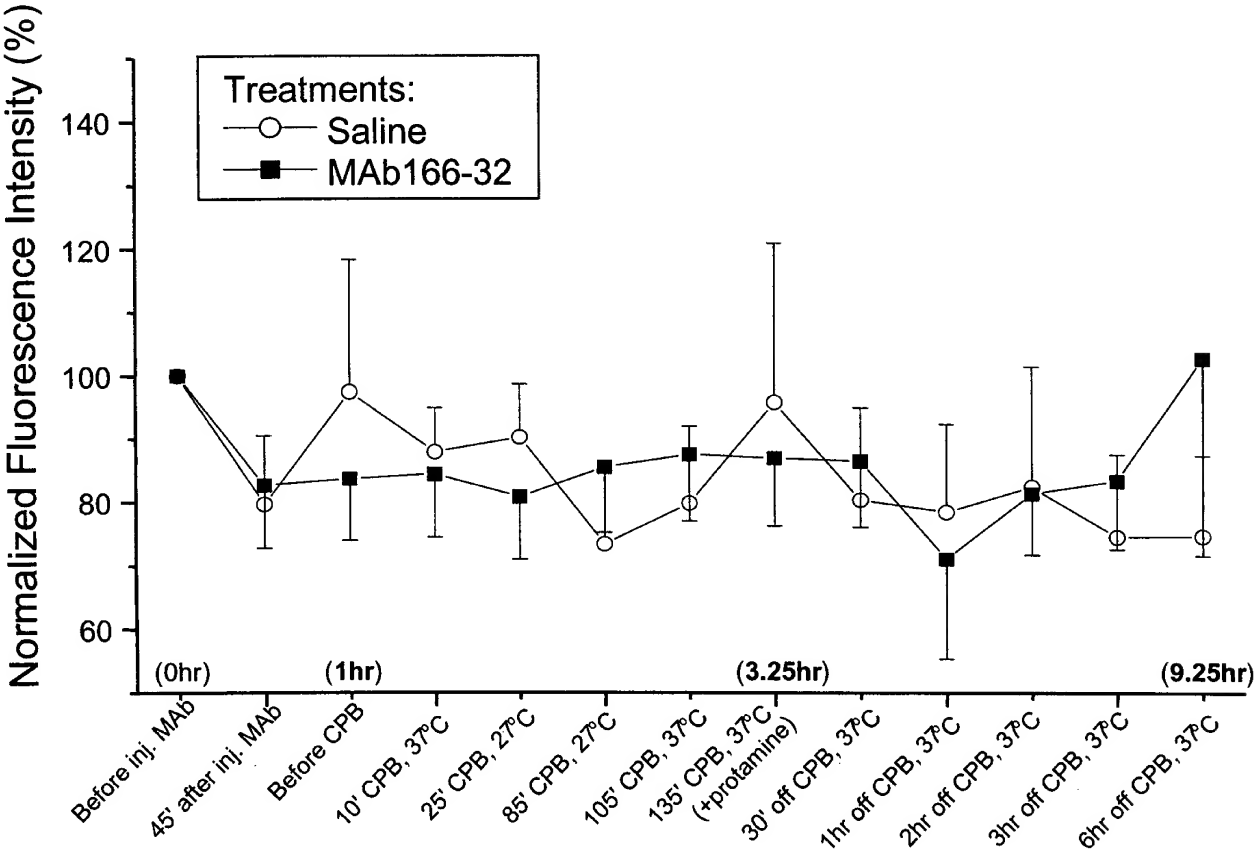

Fig. 47 Plasma IL-6 in Baboon CPB

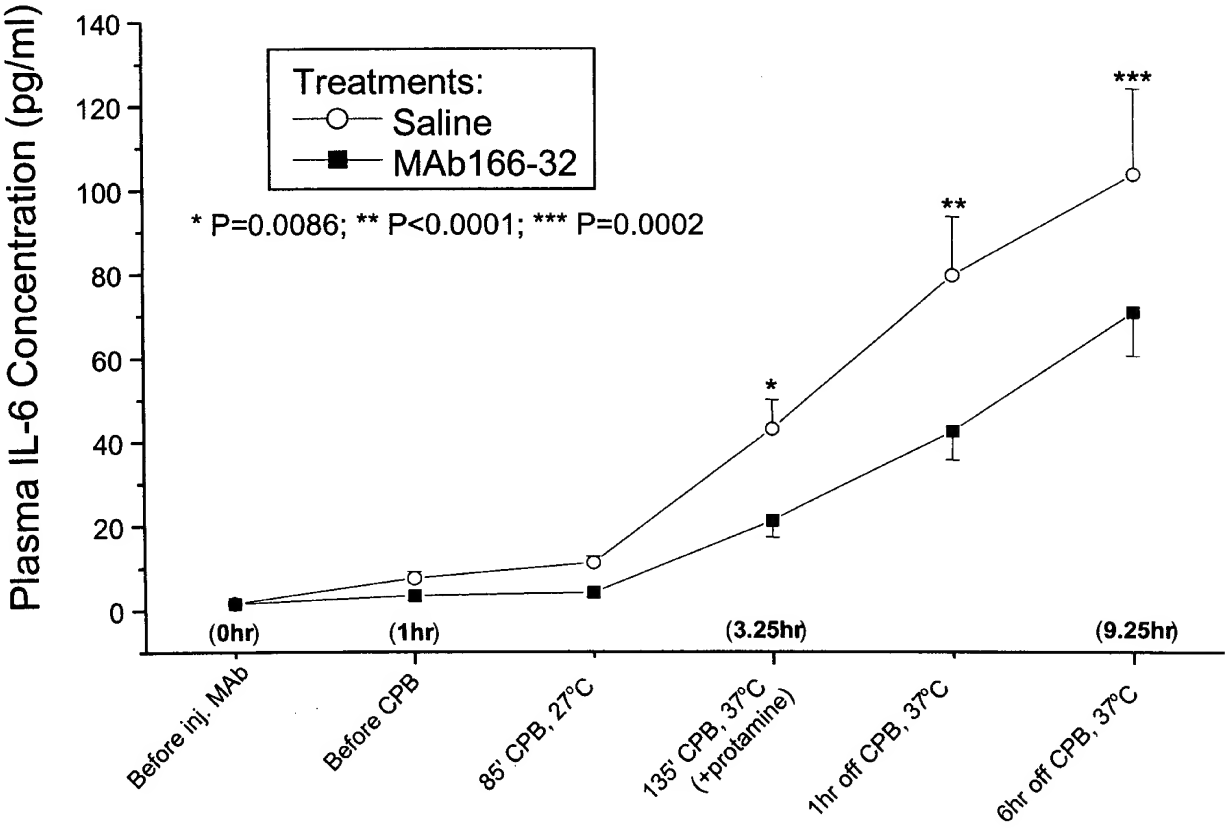

Fig. 48 Plasma LDH Level in Baboon CPB

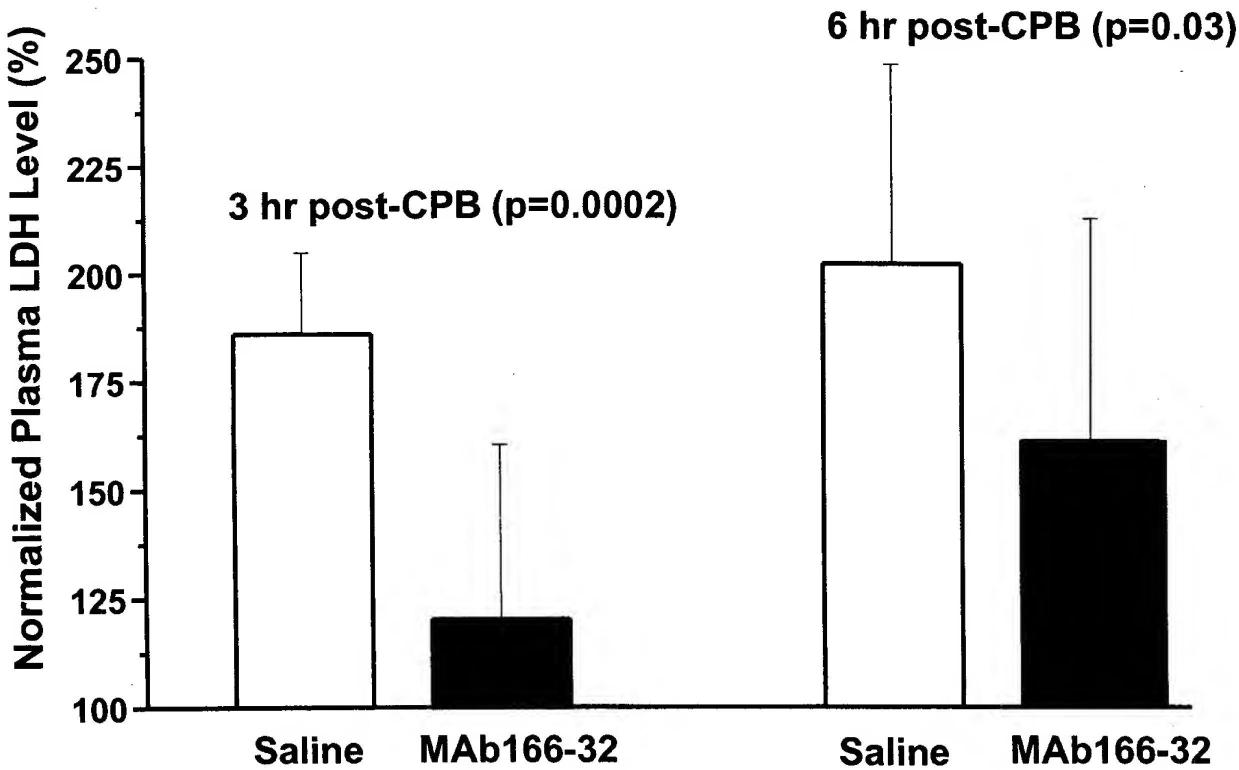

Fig. 49 Plasma Creatine Kinase (CK) Level in Baboon CPB

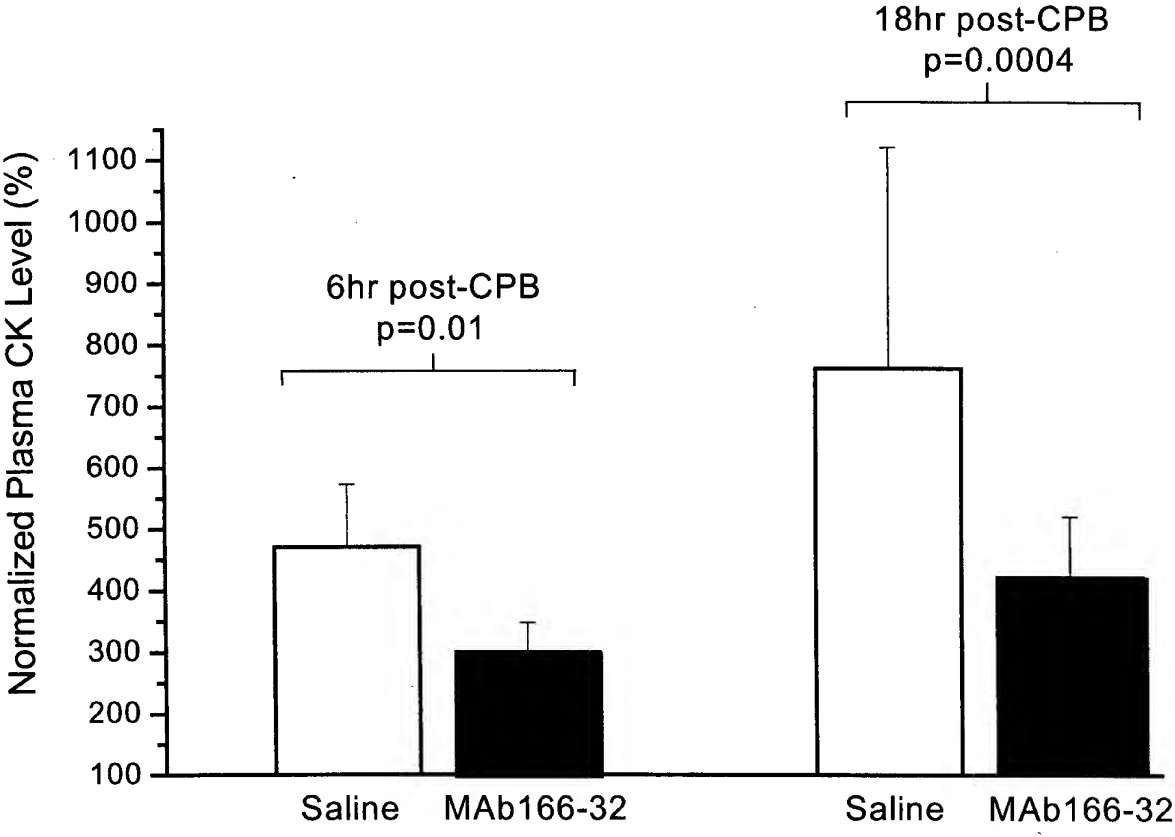

Fig. 50 Plasma Creatine Kinase Isozymes (CK-MB) in Baboon CPB

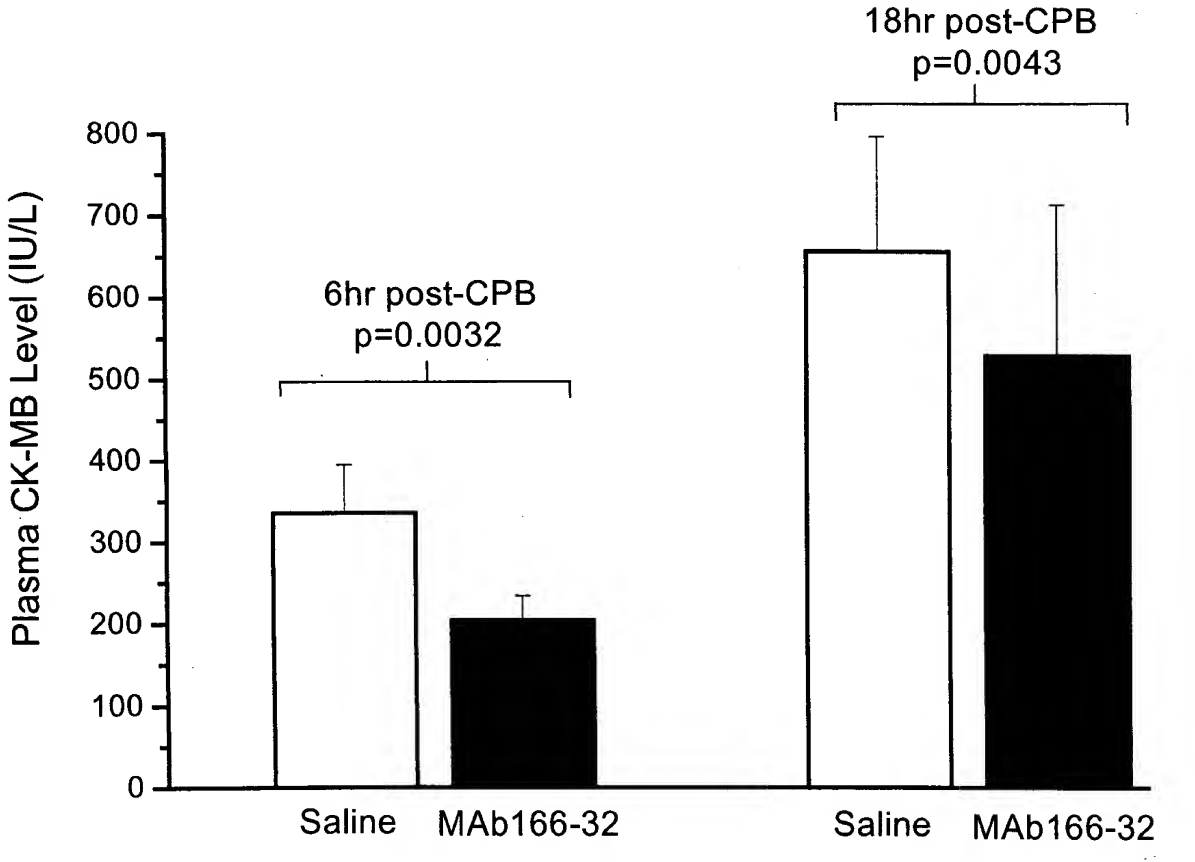

Fig. 51 Plasma Creatinine Level in Baboon CPB

(18 hr post-CPB, p=0.01)

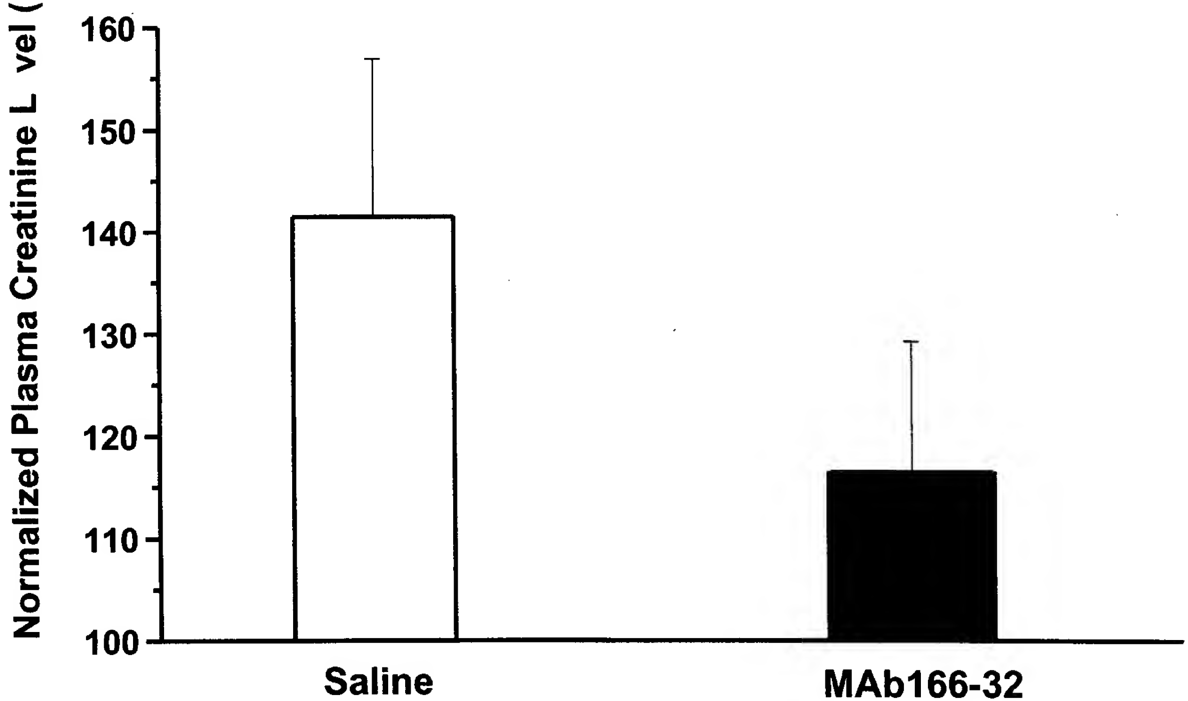

Fig. 52 Dynamic Lung Compliance of Baboons in CPB